SOURCE CHARACTERIZATION AND PRETREATMENT EVALUATION OF PHARMACEUTICALS AND PERSONAL CARE PRODUCTS IN HEALTHCARE FACILITY WASTEWATER

A Dissertation

by

PRANAV MUKUND NAGARNAIK

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

May 2011

Major Subject: Civil Engineering

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Approved by:

Chair of Committee,	Bryan Boulanger
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ABSTRACT

Source Characterization and Pretreatment Evaluation of Pharmaceuticals and Personal Care Products in Healthcare Facility Wastewater. (May 2011)

Pranav Mukund Nagarnaik, B.Tech., Nagpur University;

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Chair of Advisory Committee: Dr. Bryan Boulanger

Healthcare facility wastewaters are a potentially important and under characterized source of pharmaceuticals and personal care products in the environment. In this study, the composition and magnitude of pharmaceuticals and personal care products (PPCPs) released into a single municipality's wastewater system from a hospital, a nursing care facility, an assisted living facility and an independent living facility are presented for 54 pharmaceuticals, 8 hormones and 31 Alkylphenol ethoxylates (APEOs). Chemical oxidation using molecular ozone and advanced oxidation processes (AOPs) (UV-hydrogen peroxide, Fenton's Reagent, and Photo – Fenton's Reagent) were screened and evaluated as potential treatment technologies for removal of APEOs in water and wastewater.

In this research, APEOs were found to be the dominant PPCP class out of 94 individual analytes measured, accounting for more than 65% of the total mass loading observed leaving the healthcare facility wastewater. Seventy one out of the total measured PPCPs were detected in wastewater from at least one of the facilities.

Healthcare facilities' wastewater is the source of PPCPs in the environment; however, their contribution to the total magnitude of PPCPs in municipal wastewater and the surrounding environment will be determined by the relative flow contribution of wastewater released from the facility to the municipal sewer network. Molecular ozone and advanced oxidation processes were observed to remove APEOs from analyzed water matrices; however, understanding the product formation during the oxidation process is important before concluding a suitable treatment process. Molecular ozone reacted selectively with the double bond in the APEO, while AOPs reaction was non selective oxidation. During the AOPs, $OH^{\cdot}$ formation rate and scavenging rate constant in wastewater was found to be the factor governing the oxidation process. Thus, the research carried out informs risk management decisions concerning the prevalence of PPCPs in the wastewater, and the use of oxidation systems as treatment technologies for removal of PPCPs.

DEDICATION

To my father, Shri Mukund Nana Nagarnaik

and

my mother, Smt. Kishori Mukund Nagarnaik

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would like to thank my parents for believing in me. They not only made me realize my true potential but also supported and encouraged me to achieve that. No words can ever describe their contribution. Apart from my parents I would like to thank my loving sister Monika, my brother-in –law Pranav and my beautiful niece Saanvi for being there for me always.

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NOMENCLATURE

ACS	American Chemical Society
AOP	Advanced Oxidation Process
APEOs	Alkylphenol Ethoxylates
APs	Alkylphenols
ATC	Anatomical Therapeutic Chemical
CA	Cluster Analysis
DF	Degree of Freedom
DOC	Dissolved Organic Carbon
E_0	Oxidation Potential
EDCs	Endocrine Disrupting Chemicals
eV	Electrovolts
Fe	Ferrous Ion
FH	Fentons Advanced Oxidation Process
γ	Stoichiometric Coefficient
g/day	Grams Per Day
H_2O_2	Hydrogen Peroxide
HPLC	High Performance Liquid Chromatography
Hr	Hour
$k_{OH-H_2O_2}$	Second-Order Rate Constant of H_2O_2 With OH· ($M^{-1}s^{-1}$)
k_{OH-HCO_3}	Second-Order Rate Constant of $HCO_3$with OH· ($M^{-1}s^{-1}$)

k_{OH-DOC}	Second-Order Rate Constant of DOC With OH· ($M^{-1}s^{-1}$)
$k_{OH-tBuOH}$	Second-Order Rate Constant of t-BuOH With OH· ($M^{-1}s^{-1}$)
k_{OH-MeB}	Second-Order Rate Constant of MeB With OH· ($M^{-1}s^{-1}$)
$k_{OH-OPEO}$	Second-Order Rate Constant of OPEO With OH· ($M^{-1}s^{-1}$)
$k_{OH-NPEO}$	Second-Order Rate Constant of NPEO With OH· ($M^{-1}s^{-1}$)
kAPEO	Second-Order Rate Constant for Oxidation Of APEO
$k_{APEO,effective}$	Effective Second-Order Rate Constant of APEO With Ozone in Water Matrix
k_{O_3}	Second-Order Rate Constant for Ozone Consumption
k'_{O_3}	Pseudo First-order Rate Constant for Ozone Consumption
L/day	Liters per Day
LC/MS^n	Liquid Chromatography / Mass Spectroscopy-Ion Trap
Min	Minimum
µg/L	Microgram per Liter
µM	Micromolar
NAICS	North American Industry Classification System
ng/day	Nanograms Per Day
NP	Nonylphenol
NPEO	Nonylphenol Ethoxylate
NRMRL	National Risk Management Research Laboratory
OH·	Hydroxyl Radical
OP	Octylphenol
OPEO	Octylphenol Ethoxylate

pCBA	Para-Chlorobenzoic Acid
ppb	Parts Per Billion
PPCPs	Pharmaceuticals And Personal Care Products
R^2	Coefficient of Determination
R5CRL	Region 5's Central Research Laboratory
RMSE	Root Mean Squared Error
SIR	Single Ion Recording
SOP	Standard Operating Procedure
SSE	Sum of Squared Error
tBuOH	*Tert*-Butanol
TOC	Total Organic Carbon
UFH	Photo Fenton's Advanced Oxidation Process
UH	Ultraviolet / Hydrogen Peroxide Advanced Oxidation System
US EPA	United States Environmental Protection Agency
USGS	United States Geological Survey
UV	Ultraviolet
WWTP	Wastewater Treatment Plant

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1. INTRODUCTION TO DISSERTATION RESEARCH

1.1 Overview of Environmental Pharmaceuticals and Personal Care Products (PPCPs)

1.1.1 Prevalence

PPCPs are gathering increased attention as environmental contaminants due to their presence in wastewater effluents and potable water supplies. Because pharmaceuticals and many personal care products are intended to illicit a biological response by design, their presence in environmental and potable waters is of concern. Kolpin *et al.* first raised awareness of the widespread presence of PPCPs in environmental waters in 2000 when they reported the findings of their United States Geological Survey (USGS) national surface water quality survey [1]. The goal of their survey was to develop analytical methodologies needed to perform a screening level occurrence assessment of PPCPs in environmental waters and to determine concentrations of PPCPs in the aquatic environments. The results of the Kolpin *et al*. survey identified 80 PPCPs in 111 US waterways.

The Kolpin *et al*. dataset was followed up by a Focazio *et al*. study who performed another screening level occurrence assessment of PPCPs in source waters used for drinking water treatment using the same methodology and design from the previous USGS survey[2].

This dissertation follows the style of *Environmental Science and Technology.*

The source water survey results indicated the widespread presence of PPCPs in potable source water supplies with 63 PPCPs reported in at least one of 74 municipal source waters above parts per billion levels.

While the Kolpin and Focazio *et al*. studies continue to be the most prominent works to date concerning PPCPs as environmental contaminants, the presence of individual PPCPs in wastewater has been reported since the early 1970s. Pharmaceuticals, antibiotics[1, 3-7], anticonvulsants [2, 8-12], anti-anxiety[1, 2, 13],anti-inflammatory [8, 9, 11, 13-19], anti-psychological[20, 21], cardiovascular drugs[1, 11, 14, 21], hormones [22-30] and respiratory pharmaceuticals [1, 21, 31] have all been reported in surface water and wastewater effluents. Natural hormones, including estrogens [30, 32-37], androgens [38-41], and progestogens [22, 24, 29, 37, 39, 42] are also widely reported in the environment and wastewater effluents.

1.1.2 Risk of PPCPs as environmental contaminants

While occurrence data has demonstrated the widespread nature of PPCPs in environmental waters and treated effluents, far less is understood concerning the ecological risk of exposure to PPCPs in the environment. Because these organic compounds are designed to be biologically active, a certain risk can be anticipated for organisms exposed to environmental PPCPs even when the concentrations of PPCPs in the environment are low. For instance, several PPCPs are known to be endocrine disrupting chemicals (EDCs). The most widely studied PPCPs that are known to behave as EDCs at environmentally relevant concentrations are natural and synthetic hormones

[43-45] and alkylphenols (APs), which are degradation products of alkyphenol ethoxylates (APEOs) widely used in detergents.

Hormones, including prescription hormones, have demonstrated biological receptor impacts below 5 parts-per-trillion [28]. Their presence in treated effluents leaving wastewater treatment systems contribute to the adverse physiological effects noted in fish downstream from wastewater effluent discharges [30, 46-48]. The estrogenicity of APs is also established, with octyl- or nonyl- phenol being the most estrogenic. While APs are far less potent than hormones in their effect on the estrogen receptor of exposed organisms, AP concentrations in wastewaters are normally three orders of magnitude higher than hormone concentrations. Therefore, the relationship between a compound's potency and concentration is important to consider. In addition to hormones and alkylphenols, many other PPCPs are assumed to be EDCs, however, their direct ecological impacts at environmentally relevant concentrations are disputed.

The risk to humans from exposure to PPCPs (including the EDCs mentioned in the past paragraph) in environmental waters is more disputed than the ecological risks of PPCP exposure. Although the presence of pharmaceuticals at the parts-per-trillion levels in the drinking water does not currently appear to pose a direct adverse risk to humans, indirect impacts from some pharmaceuticals are documented and need to be considered. For instance, Guardabassi *et al.* demonstrated that discharges containing hospital wastewater increased the prevalence of oxytetracycline-resistant isolates among 385 strains of *Acinetobacter* in monitored environmental systems [49]. Reinthaler *et al.*

showed similar impacts of hospital wastewaters on multiple antibiotic resistance of 767 isolates of *E. coli* in samples wastewater treatment plants [50].

Hartmann *et al*. have also reported that fluoroquinolone antibiotics have shown mutagenic and carcinogenic genotoxicity at environmentally relevant concentrations [51]. While the exact mechanisms of transferring antibiotic resistance due to the influence of hospital wastewater is an area of current research, it is known that antibiotic resistant genes can also be transferred horizontally by conjugation through cell-to-cell contact or by transformation when resistant plasmid DNA is transferred into bacteria [52]. Therefore, indirect impacts, such as development of antibiotic resistant bacteria, must be considered while assessing potential risk of environmental pharmaceuticals.

Indirect impacts of other PPCPs on human health are more difficult to determine. Limited toxicology studies of chronic exposures exist to assess low level, long term exposures to anticonvulsants, antidepressants, antihypertensives, or cytostatics pharmaceuticals in the most utilized animal-humans models. Their presence in the potable water supply is, therefore, a highly controversial and debated topic.

1.1.3 Healthcare facilities as sources of PPCPs to municipal wastewater

Contamination of environmental waters with PPCPS is widespread and our understanding of associated exposure risks is limited. As a precautionary measure, risk management efforts to characterize sources of PPCPs to environmental systems and promote removal of PPCPs from known release points are needed. Source characterization data for important societal sources of PPCPs that contribute to municipal wastewater loadings is lacking. Use data of PPCPs is also difficult to obtain

across sectors of society or on an individual community/household basis. However, the healthcare sector controls the flow of prescription pharmaceuticals to patients and administers doses at much higher levels than are usually prescribed to the general public. Healthcare facilities also administer hormone therapy using natural and synthetic hormones. These facilities also are consumers of detergents used in house to launder linens. Therefore, healthcare facilities are a logical starting point when attempting to characterize important social sources of PPCPs released to municipal wastewater treatment systems.

In the United States there are approximately 9,178 general medical and surgical hospitals (North American Industry Classification System (NAICS) Code: 622110), 21,459 nursing care facilities (NAICS Code: 623110), 6,843 continuing care retirement communities (NAICS Code: 623311) and 3,491 homes for elderly (NAICS Code: 623312) providing healthcare services to millions of patients [53]. The importance of these healthcare facilities as a potential point source contributor of PPCPs to municipal wastewater systems is widely anticipated, but there is a lack of information in the literature regarding the concentration and magnitude of PPCPs in the wastewater from these facilities.

Starting in the mid 1980s, researchers began developing methods to determine the concentration of individual pharmaceutical classes in hospital effluents that were released either due to patient excretions or disposal practices of expired pharmaceuticals. Kummerer et al. investigated chemotherapeutic platinum-based compounds, which was the first class of pharmaceutical compounds investigated. Platinum-based

pharmaceuticals were detected in the wastewater from one hospital within a concentration range of 10 – 610 ng/L platinum [54]. Later Mahnik *et al.* furthered the earlier work of Kummerer et al. when they reported the presence of antineoplastic agents for cancer treatment (non-platinum based drugs) in the wastewater effluents of a hospital [55-58]. Mahnik *et al*. reported a concentration level ranging from 8.6 – 124 μg/l for doxorubicin, eprubicin and daunorubicin [59].

Following the work of Herberer and Mahnik, Brown *et al*. evaluated the presence of eleven antibiotics in effluents from a hospital, residential area, dairy and a wastewater treatment plant[59]. Antibiotic concentrations for ofloxacin, trimethoprim and sulfamethaxazole in hospital wastewater were reported to be 36, 2.9, and 2.1 μg/L, respectively [3]. Gomez *et al*. expanded the list of known pharmaceuticals in hospital wastewaters by reporting the presence of codine (analgesic), atenolol (cardiovascular), ranitidine (gastroenterological), metronidazole (antibiotic) and ketorolac (analgesic) in the wastewater from a small hospital with concentrations of the individual analytes ranging from 0.06 – 151 μg/L [16, 60].

While determining the concentration of pharmaceuticals in hospital effluents is timely, concentration data alone does not allow for the characterization of hospital effluents as sources of pharmaceuticals to the environment. In order to characterize hospitals as a source, flow data needs to be integrated to determine a mass loading of pharmaceuticals from these facilities. Heberer *et al*. were the first group to undertake a mass loading calculation. In 2005 they published a report exploring the concentration and mass loading of carbamazepine (an antiepileptic) in wastewater from a military

hospital. Their findings indicate a total mass loading of carbamazepine leaving the hospital to be 4 – 460 grams per week [61].

From the limited source characterization data available in the literature, it is apparent that hospitals do release some pharmaceuticals to municipal sewer systems. However, hospital effluents have not been evaluated for the presence of many of the most commonly prescribed pharmaceuticals or for other personal care products. Additionally, while the presence of PPCPs in other types of healthcare facilities is anticipated, the PPCP concentration and magnitude in other types of healthcare providing facilities is not previously reported.

1.1.4 Pretreatment of healthcare facility wastewaters as a risk management approach

Because of the anticipated occurrence of PPCPs in healthcare facility wastewaters it is important to consider the available options that exist for implementation of PPCP pretreatment technologies at identified sources. Pretreatment options of interest include physical, chemical, and microbial based treatment processes. However, due to the risk of developing antibiotic resistant bacteria, microbial based treatment technologies should be considered as a last-resort option.

Physical-chemical treatment processes such as nano-filtration, reverse osmosis, oxidation and advanced oxidation demonstrate proven potential to separate or oxidize organic contaminants in aqueous systems [62, 63]. For pretreatment on-site, however, advanced oxidation has greater promise due to its smaller space requirement and lower initial cost. Because of the scalability and cost of advance oxidation processes, there has

been a steady increase in the number of articles appearing in the literature regarding the evaluation of different AOPs for removal of PPCPs over the past decade.

Despite the growing literature, only one study to date reports on the effectiveness of an advanced oxidation technology to degrade a PPCP (ciprofloxacin) using real hospital effluent samples as the test matrix. In their study, ciprofloxcin with an initial concentration of 200 μg/L was completely destroyed within 1 hr using a heterogeneous photocatalytic process [64]. The remainder of related literature is full of reports of AOPs that have been evaluated based upon spiking PPCPs into distilled water or drinking water samples [64]. In all cases, only a limited amount of analytes were evaluated at a time. In order to understand the actual effectiveness of existing oxidation technologies, evaluations should be done with real samples to evaluate matrix competition for the oxidants.

1.2 Research Plan

After a collective evaluation of the literature, this project was planned to develop source characterization data for PPCPs in healthcare facility wastewaters and to evaluate the performance of oxidation technologies to remove a selected class of PPCPs from water and wastewater. The following two hypotheses were defined to guide this risk management based research:

1.2.1 ***Hypothesis 1****: Healthcare facilities are a source of PPCPs to municipal wastewaters.*

Wastewaters from four different healthcare facilities (including a hospital, an assisted living facility, an independent living facility, and a nursing home) within the same municipality were evaluated for 54 pharmaceutical analytes, 29 APEOs, two APs, and nine hormone analytes. The importance of hypothesis 1 was to motivate work to obtain a comprehensive dataset that can be used to characterize healthcare facilities as a source of PPCPs to municipal sewer systems. Also, the majority of these analytes have never been reported in healthcare facility effluents prior to this dissertation research.

1.2.2 ***Hypothesis 2:*** *Chemical oxidation processes can be used to remove APEOs from water and wastewater.*

Chemical oxidation systems that use molecular ozone and/or the hydroxide radical were screened and evaluated as potential treatment technologies for removal of APEOs in water and wastewater. APEOs were selected for further study because this class of personal care products is commonly used in commercial detergents and demonstrates endocrine disrupting properties at environmentally relevant concentrations. APEOs were also identified at the high concentrations within the healthcare facility effluents evaluated by research motivated by Hypothesis 1 and their removal using oxidation technologies has not been previously reported.

The removal of APEOs using ozone, Fenton's reagent, ozone-hydrogen peroxide, and UV-hydrogen peroxide was evaluated in laboratory water in order to determine the reaction kinetics, stoichiometry, and product identification in order to clarify the reaction

mechanism. The oxidation technologies were also evaluated for their ability to remove APEOs in water and wastewater collected from the field to explore the effect of the matrix on kinetics. Samples were collected from tap water, hospital effluent, wastewater treatment plant influent, and wastewater treatment plant effluent. Collectively, these oxidation process evaluations inform risk management decisions concerning the use of oxidation systems as pre-treatment technologies for source reduction of PPCPs at healthcare facilities or other sources of PPCPs to municipal wastewaters.

1.3 Organization of this Dissertation

This dissertation has been organized as a collection of six papers collected together and presented in individual sections. Section 1 presents an overview of environmental PPCPs, provides the research plan, and explains the organization of the dissertation. Section 2 summarizes each of the four papers on source characterization of healthcare facilities completed to evaluate Hypothesis 1. Three of the four papers are published in peer-reviewed journals and the fourth paper is currently submitted and undergoing the peer review process. Section 2 provides an overview of these four papers and presents additional statistical analysis of the data that is not found within the published/submitted papers.

Section 3 presents a submitted paper currently in peer-review at Chemosphere concerning the reaction of APEOs with hydroxide radicals generated through different advanced oxidation techniques. Section 4 presents a submitted paper concerning the reaction of APEOs with molecular ozone also in review at Chemosphere. Both papers include an exploration of reaction kinetics, stoichiometry, and metabolism identification

to clarify the reaction mechanism of APEOs with oxidation systems potentially used for pretreatment purposes. Both papers present research carried out in laboratory and field waters (aqueous environmental matrices) that also explore the impact on the matrix on removal of APEOs from the sample.

The dissertation concludes with Section 5, where conclusions from the study and suggestions for possible future directions of research are presented along with a few lessons learned and parting thoughts.

2. SCREENING LEVEL ASSESSMENT OF HEALTHCARE FACILITIES AS SOURCES OF PPCPS TO MUNICIPAL WASTEWATERS

2.1 Introduction

While the presence of these pharmaceuticals and EDCs in the environment is established, sources of these compounds to the environment are less well characterized. Healthcare facilities are a potentially important source of EDCs and pharmaceuticals to the environment that are particularly under characterized.

The primary aim of this section is to detail research concerning our hypothesis that all healthcare facilities, including but not limited to hospitals, are sources of PPCPs to the municipal wastewater systems. This section provides a summary of four papers that assess the concentrations and magnitude of environmental loadings of nine natural and synthetic steroid hormones, 29 APEOs, two APs, and 54 pharmaceuticals from four different healthcare facilities. These papers include:

- Nagarnaik, P.M., M.A. Mills, and B. Boulanger, *Concentrations and mass loadings of hormones, alkylphenols, and alkylphenol ethoxylates in healthcare facility wastewaters.* Chemosphere, 2010. **78**(8): p. 1056-1062.
- Nagarnaik, P., A. Batt, and B. Boulanger, *Concentrations and mass loadings of cardiovascular pharmaceuticals in healthcare facility wastewaters.* Journal of Environmental Monitoring, 2010. **12**(11): p. 2112-2119.
- Nagarnaik, P., A. Batt, and B. Boulanger, *Source characterization of nervous system active pharmaceutical ingredients in healthcare facility wastewaters.* Journal of Environmental Management, 2011. **92**(3): p. 872-877 and

- Nagarnaik, P., A. Batt, and B. Boulanger, *Healthcare facility effluents as a point source of selected pharmaceuticals to municipal wastewater.* Water Environment Research, Sumitted.

Collectively, these four papers provide an estimation of daily mass loadings contributed by a multi specialty hospital, multi care skilled nursing facility, an assisted living facility, and an independent living facility located within a single municipality in Texas. The papers were split up for publication based upon the peer-review process feedback and the methods used to measure each of the respective analyte classes across three United States Environmental Protection Agency (US EPA) laboratories. This section provides a summarized report of the findings in order to provide insight on the relative contributions and magnitudes of analyzed PPCPs released to municipal wastewater systems from healthcare facilities monitored within this dissertation research.

2.2 Experimental

Experimental details are provided within each paper, but are summarized in brief below [65-67]. A description of the four different healthcare facilities within a single municipality in Texas that were sampled during our research is provided in Table 2-1. Please note that all facility names are withheld to protect the location identities. Twenty-four hour composite samples of each facility's wastewater effluent were collected and analyzed using an ISCO autosampler. The ISCO sampler collected 100 ml of wastewater every 15 mins for 24 h and stored it in an ice-chilled 10-L polypropylene bottle. The collected samples from each facility were then sub-sampled using a

peristaltic pump into 1 L pretreated amber glass bottles in the field and shipped to the corresponding EPA laboratories for analysis.

Table 2-1 Description for each healthcare facility sampled in this study

Facility Name	**NAICS Name and Code**	**# of Beds**	**Wastewater Flowrate**	**Description of Services**
Hospital	General medical and surgical hospital, 622110	375	500,000 L/day	in patient general hospital care, coronary care, surgical, and intensive care; outpatient cardiac, orthopedic, obstetrics and gynecology, pulmonary, surgical, gastrointestinal and respiratory care
Nursing Care	Nursing care facility; 623110	300	100,000 L/day	nursing care, physical rehabilitation, Alzheimer's care, and hospice
Assisted Living	Continuing care retirement communities, 623311	225	50,000 L/day	custodial non-medical care, as well as personalized medical care including medication management services, Alzheimer's care, and short-term skilled nursing care
Independent Living	Homes for elderly (NAICS:623312)	225	70,000 L/day	short-term custodial non-medical care services and limited healthcare services in the area of onsite therapy, wellness, and rehabilitation providers

2.2.1 Analytical methods

Four different analytical techniques were used for the analysis of steroid hormones, long-chain APEOs, short-chain APEOs, APs and pharamceuticals. Table 2-2 and Table 2-3 provide a summary of all individual analytes measured in this study. All analyses were performed using laboratory standard operating procedures developed in accordance with EPA's quality assurance program. All analytical data presented in this study was corrected to account for matrix effects based upon the matrix spike recovery controls present within each independent method.

All hormone samples were extracted and analyzed according to US EPA's National Risk Management Research Laboratory's (NRMRL) "Standard Operating Procedure (SOP) for the Analysis of Steroid Hormones in Aqueous Samples (Revision 4r)". This SOP details the extraction and analysis of eight hormones: 17β-estradiol, estrone, estriol, 17α-ethynylestradiol, testosterone, androstenedione, progesterone, and dihydro-testosterone. The SOP used to analyze the hormones is similar to the procedure previously reported by Esperazna et al. [29]. The acceptable surrogate recovery was between 60 and 140%. All long-chain APEO samples were analyzed using US EPA's Region 5 Central Research Laboratory's SOP MS006 V1 ("Laboratory for analysis of nonylphenol polyethoxylates (NPnEO, $3 \leq n \leq 18$) and octylphenol polyethoxylates (OPnEO, $2 \leq n \leq 12$) in wastewater samples using selected ion recording liquid chromatography / mass spectrometry (LC/MS)"). The detailed description of the method is provided elsewhere [65-67]. The acceptable range of matrix spike recovery was defined to be between 60 and 140%. All AP and short-chain APEOs were analyzed

using ASTM D7065-06 ("Standard Test Method for Determination of Nonylphenol, Bisphenol A, p-tert-Octylphenol, Nonylphenol Monoethoxylate and Nonylphenol Diethoxylate in Environmental Waters by Gas Chromatography Mass Spectrometry") [68]. The acceptable range of matrix spike recovery was defined to be between 60 and 140%.

Table 2-2 Pharmaceuticals measured in this study grouped by the Anatomical Therapeutic Chemical (ATC) classification system

ATC Code A: Alimentary tract and metabolism	
Cimetidine	A02BA01
Ranitidine	A02BA02
Glyburide	A10BB01
Glipizide	A10BB07
ATC Code B: Blood and blood forming organs	
Warfarin	B01AA03
ATC Code C: Cardiovascular system	
Clonidine	C02AC01
Hydrochlorothiazide	C03AA03
Furosemide	C03CA01
Triamterene	C03DB02
Fluocinonide	C05AA11
Propranolol	C07AA05
Metoprolol	C07AB02
Atenolol	C07AB03
Amlodipine	C08CA01
Verapamil	C08DA01
Norverapamil*	C08DA01

Table 2 – 2 continued

ATC Code C: Cardiovascular system	
Diltiazem	C08DB01
Desmethyldiltiazem*	C08DB01
Enalapril	C09AA02
Valsartan	C09CA03
Simvastatin	C10AA01
Atorvastatin	C10AA05
Gemfibrozil	C10AB04
ATC Code G: Genito-urinary system and sex hormones	
Norethindrone	G03AC01
Testosterone	G03BA03
Progesterone	G03DA04
ATC Code H: Systemic hormonal preparations, excluding insulins	
Betamethasone	H02AB01
Methylprednisolone	H02AB04
Prednisolone	H02AB06
Prednisone	H02AB07
Hydrocortisone	H02AB09
ATC Code J: Antiinfectives for systemic use	
Trimethoprim	J01EA01
Sulfamethoxazole	J01EC01
ATC Code M: Musculo-skeletal system	
Ibuprofen	M01AE01
2-hydroxy-ibuprofen*	M01AE01
ATC Code N: Nervous system	
Oxycodone	N02AA05
Propoxyphene	N02AC04
Acetaminophen	N02BE01
Carbamazepine	N03AF01
Benzatropine	N04AC01
Alprazolam	N05BA12

Table 2 – 2 continued

ATC Code N: Nervous system	
Amitriptyline	N06AA09
10-hydroxy-amitriptyline*	N06AA09
Fluoxetine	N06AB03
Norfluoxetine*	N06AB03
Paroxetine	N06AB05
Sertraline	N06AB06
Desmethylsertraline*	N06AB06
Amphetamine	N06BA01
ATC Code R: Respiratory system	
Albuterol	R03AC02
Fluticasone	R03BA05
Theophylline	R03DA04
Hydrocodone	R05DA03
Promethazine	R06AD02

* compounds are metabolites. For the metabolites the same ATC code as the parent compound is listed.

Table 2-3 Hormones and APs/APEOs measured in this study

Hormones	APs/APnEOs*	
Androgens	Octylphenol	Nonylphenol
Androstenedione	OP2EO	NP3EO
Dihydrotestosterone	OP3EO	NP4EO
Testosterone	OP4EO	NP5EO
Estrogens	OP5EO	NP6EO
Estriol	OP6EO	NP7EO
Estrone	OP7EO	NP8EO
17 α-ethynylestradiol	OP8EO	NP9EO
17 β-estradiol	OP9EO	NP10EO
Progestagens	OP10EO	NP11EO
Progesterone	OP11EO	NP12EO
	OP12EO	NP13EO
		NP14EO
		NP15EO
		NP16EO
		NP17EO
		NP18EO

* APnEO represents an alkyl phenol ethoxylate with an ethoxylate chain length of n

Specific details of the pharmaceutical preparation, extraction, and analysis are presented elsewhere [65, 67, 69]. Pharmaceutical samples were extracted with 150 mg Oasis HLB MCX cartridges® and were analyzed using a Waters Aquity ultra performance liquid chromatography coupled to a Micromass Quattro Micro triple quadrupole mass spectrometer. The acceptable target recoveries were set between 60% and 140%. For presentation purposes, pharmaceuticals were classified based upon the first level of the Anatomical Therapeutic Chemical (ATC) classification system. This classification system is used to group pharmaceuticals based upon their target organ or system. Analyte classification became necessary in order to interpret data and facilitate discussion.

The analyzed pharmaceuticals were distributed across 9 of the 14 therapeutic categories within the ATC system as given in Table 2-2.

2.2.2 Mass loading

The average daily and monthly flow rates from each facility were obtained from the municipality where the samples were acquired. The total mass loading from each facility was calculated by multiplying individual analyte concentrations in the composite sample from each facility composite by the average daily flow for that facility. The estimated mass loadings are reported as ng/day for the hormone analytes and pharmaceuticals and g/day for the APEO analytes.

2.2.3 Statistical analyses

Matlab™ was used to organize analyte concentration data by site and to perform the statistical analysis. The data was first checked for normality using the Shapiro-Wilk test and then checked for equality of variance using Lavene's test. The data was found to be non-normal and unequal in variance and a non-parametric analysis was used to interpret the statistical relationships between composites. For non-parametric analysis, a post hoc two-way Friedman's ranks test was performed first, followed by step-wise multiple comparisons tests. The non-parametric method used in the data analysis was selected to control for a potential increase of the type I error caused by multiple comparison testing. Only analytes that were present in at least one of the four composites were included in the statistical analysis. Analytes that were present at one site and nondetectable at another had their non-detect concentration set to zero in order to perform the statistical analysis.

Cluster analysis (CA) was performed in order to further understand the relative similarities between the sites. The multivariate cluster analysis classifies and groups the objects based on the similarities within the system. Hierarchical clustering forms the clusters in a sequential manner with a decreasing similarity of subgroups merged into a single cluster. CA was applied to wastewater from all healthcare facility and PPCP concentrations using a single linkage method. Each analyte concentration is considered as a data point and the minimum distance between two sites is calculated by:

$$D(A,B) = \min\{d(x_i, x_j), for\ x_i in\ A\ and\ x_j\ in\ B\} \quad 2\text{-}1$$

Where $d(x_i, x_j)$ is the Euclidean distance, x_i and x_j are the concentrations for each analyte at the paired sites, and A and B are the pair of sites. At each step the distance is found for every pair of the clusters and the two clusters with smallest distance are merged. After two clusters are merged the procedure is repeated for the next step. The result of a hierarchical clustering procedure can be displayed graphically using a tree diagram, also known as a dendrogram, which shows all the steps in the hierarchical procedure and the resulting relationships between PPCP concentrations between sites.

2.3 Summary of Source Characterization Papers' Results and Discussions

2.3.1 PPCP composition in healthcare effluents

Table 2-4 represents the frequency of detection of analytes within the four healthcare facility wastewater composite samples broken down and grouped into pharmaceutical, hormone, and AP/APEO analytes. The hospital had the highest measured occurrence of all the analytes, followed by the independent living facility, the nursing facility, and the assisted living facility.

Table 2-4 Frequency of detection at four healthcare facilities wastewaters

Facility	# Pharmaceutical	# Hormones	# APs/APEOs	# Total
Hospital	37/54	7/9	22/31	66/94
Nursing Facility	36/54	7/9	13/31	56/94
Assisted Living	22/54	4/9	16/31	42/94
Independent Living	38/54	5/9	15/31	58/94

The mean concentration and relative standard deviation of PPCPs analyzed in four healthcare facility wastewaters can be found for each analyte within the individual papers [65-67]. In summary forty-one out of the 54 measured pharmaceutical analytes were detected in at least one site. Out of the total targeted 54 pharmaceuticals, 39% were detected in all four sampled sites. Analyte percent recovery in the matrix spike recovery (MSR) samples varied by analyte in each sample matrix. Matrix spike recovery was within the acceptable target range (60% - 140%) for 73% of all analytes, less than 60% for 11% of all analytes, above 140% for 6.5 % of all analytes, and unable to be determined due to the high magnitude of the analyte present in the sample for 4% of the analytes. The analyte with the maximum mean concentration for each ATC classified code group was ranitidine (0.9 μg/L) for ATC Code A; warfarin (0.07 μg/L) for B; valsartan (14.6 μg/L) for C; hydrocortisone (0.4 μg/L) for J; ibuprofen (30 μg/L) for M; amitriptyline (0.3 μg/L) for N; and hydrocodone (0.2 μg/L) for R. Thirteen pharmaceutical analytes were not detected in any of the sampled facility's wastewaters.

The hospital, nursing care facility, assisted living and independent living had 7, 6, 4 and 6 individual pharmaceutical analytes present at concentrations higher than 1 μg/L.

Seven out of the eight analyzed steroid hormones were detected in at least one of the facility composite samples. Androstenedione and progesterone were found in wastewater from all of the healthcare facilities with a concentration range from 9 ng/L progesterone in the independent living facility composite to 127 ng/L androstenedione in the hospital's composite sample. Overall, the hospital composite sample had the highest measured concentration of each hormone analyte, except for 17β-estradiol. The maximum concentration of 17β-estradiol was nominally higher in the nursing care facility. Perhaps surprisingly, the synthetic 17α-ethynylestradiol was not observed in any of the facility composites.

For APs and APEOs, nonylphenol (NP) and octylphenol (OP) were not detected. For the monoethoxylate and diethoxylate nonyl- and octylphenols surrogate recoveries did not meet QA/QC limits, therefore, they are not reported although no presence of these compounds was evident during analysis.

All NPEO and OPEO chain lengths, Σ(NPnEO, $3<n<18$) and Σ(OPnEO, $2<n<12$), respectively, were summed to give the total concentration discussed here. The sum of NPEO ($3<n<18$) will be identified as ΣNPEO and the sum of OPEO ($2<n<12$) will be identified as ΣOPEO. The concentrations of ΣNPEO are an order of magnitude higher than of ΣOPEO for the facility composites. Overall, the assisted living facility composite had the highest ΣNPEO concentrations (258 μg/L), followed by the hospital composite (111 μg/L), the independent living facility composite (26 μg/L), and the

nursing facility composite (19 μg/L). The hospital composite had the highest concentration of ΣOPEO (13 μg/L) followed by multi care nursing care facility (2 μg/L). ΣOPEO were not detected in the assisted living or independent living facility composites.

The higher incidence and magnitude of NPEO compared to OPEO in this study appear to be supported by production estimates. Approximately 80% of the total APEOs used as surfactants are NPEOs [47, 48, 70]. The presence of all long-chain APEOs (n>2) and lack OP and NP is also of interest. The high amount of long-chain APEOs dominating the healthcare facility wastewaters sampled in this study signifies a source signature as APEOs in detergents degrade to APs during the wastewater treatment process. The presence of NPEOs distributed in chain lengths from eight to three may indicate that breakdown of the APEO chain length begins to occur at the source.

2.3.2 PPCP mass loading estimates in healthcare effluents

The overall mass loading of PPCPs in a facility's wastewater was estimated in order to understand the relative importance of healthcare facilities as a source of different groups of PPCPs. Figure 2-1 illustrates the relative contribution of total pharmaceuticals, APs/APEOs and hormones within each healthcare facility wastewater using pie charts. The size of the pie chart indicates the total mass loading of all measured PPCPs within each facility relative to each other. Maximum mass loading of total PPCPs was found in effluents from the hospital (94 g/day) followed by that from the nursing care facility (26 g/day), assisted living facility (13 g/day) and independent living facility (11 g/day).

At the hospital, assisted living, and independent living facilities, APs/APEOs contributed to more than 65% of the total mass loading of PPCPs, signifying the importance of this compound class within healthcare facilities. Within the nursing care facility, pharmaceuticals had the highest contribution followed by APs/APEOs.

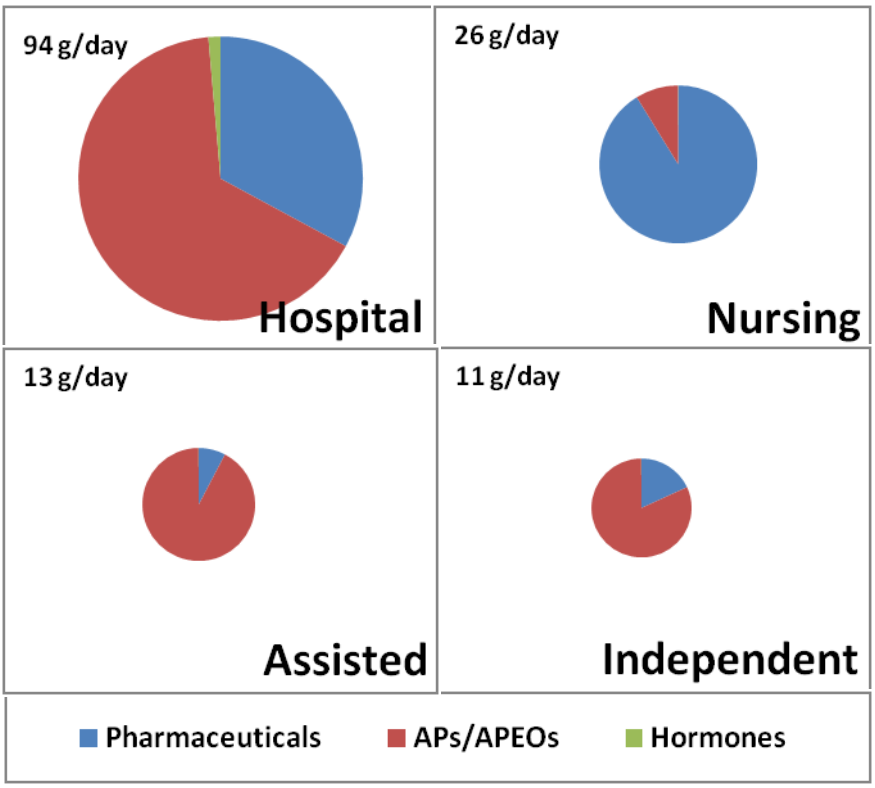


Figure 2-1 Relative contribution of analytes to wastewater loadings for each healthcare facility. The total mass loading (g/day) observed for each facility is also presented.

The estimated mass loading of pharmaceuticals from each facility was 1.1 g/day from the assisted living facility, 2.2 g/day for independent living facility, 24 g/day from the nursing care facility, and 31 g/day from the hospital with a combined pharmaceutical mass loading from all facilities of ~58 g/day.

Five pharmaceutical analytes could explain 80% or more of the total pharmaceutical loading at each location. The large contribution of five pharmaceutical analytes is of interest for risk management purposes and appears to follow logically from the type of healthcare treatment occurring at each facility. It is of interest that the four highest contributors of pharmaceutical mass loading (from our analyte sets) in the assisted living facility and independent living facility are all cardiovascular medications, whereas the top five pharmaceutical contributors in the multi-care nursing facility were two anti-infectives and three of the measured cardiovascular medications. The presence of pain medications and high amounts of anti-infectives is perhaps no surprise for a facility that covers many levels of healthcare from skilled nursing to hospice. High daily flow from the hospital facility explains the higher magnitude of pharmaceutical released when the hospital is compared to the other facilities.

The estimated total mass loading of APEOs from all facilities indicates that healthcare facilities may be a significant point source contributor of APEOs (and thus APs) to the municipal wastewater system. The total mass loading of APEOs from all facilities was estimated to be 70 g/day. The hospital contributed approximately 80% of the total mass loading of APEOs from all facilities with 54 g/day leaving the hospital. This finding highlights the importance of understanding mass loadings of analytes. The

concentration of APEOs in the assisted living facility wastewater composite sample was more than two times higher than in the hospital wastewater composite sample. However, the hospital's daily wastewater flow (500,000 L/day) was ten times higher than the assisted living facility's flow (50,000 L/day). In order to make risk management decisions, characterization data presented in the literature must include flow data from each source in order to determine mass loadings.

The hormone mass loadings from the healthcare facilities are three orders of magnitude lower in comparison to the APEO loadings. The estimated total mass flow of hormones ranged from 92 mg/day at the hospital to 2 mg/day at the assisted living facility. The overall androgen contribution to the total mass loading of hormones was more than 65% at all the facilities, with androstenedione contributing more than 40% of the observed mass loading for each site. With such a small mass loading of steroid hormones, it appears unlikely that healthcare facilities are a significantly elevated source of hormones to municipal wastewater systems. This result is partially surprising, because the hospital wastewater included wastewater from a labor and delivery unit. However, an elevated estrogen signal was not observed.

2.3.3 Statistical analysis

The concentration data within each composite were determined to be non-normally distributed for each sampled facility. Therefore, non-parametric Friedman's methodologies were used to evaluate statistical relationships occurring between PPCPs concentrations from each healthcare facility wastewater. Friedman's test does not treat the two composite sites symmetrically and it does not test for any interaction between

two sites, instead it is a test to evaluate the difference between each sampled facility's observed concentrations.

The Friedman test begins by rank–ordering the measures for each analyte concentration. The null hypothesis in this scenario is that the four different healthcare facilities' do not differ with respect to the concentration of analytes. The statistical analysis showed that there wasn't a significant difference between four healthcare facilities' wastewater ($p=0.1972$) with respect to summed pharmaceutical concentrations. However a significant difference was observed between at least one of the four healthcare facilities' wastewater for hormones ($p = 0.007$) and APs/APEOs ($p < 0.0001$). In order to further understand the differences within the healthcare facilities, multiple comparison tests were performed using the statistical information obtained from Friedman's test. This results in a pair wise comparison of each facility. Figure 2-2 displays a graph for the estimates with the intervals around them. The symbol represents the mean rank of each facility, while the solid line represents the 95% confidence interval about the mean. In this approach two means are significantly different if their intervals are disjoint and not significantly different if their intervals overlap. The Multiple Comparison Test reveals that there is no significant difference between all the healthcare facilities for pharmaceutical analytes grouped together. For hormones, the assisted and independent living facility hormone concentrations were significantly different and lower than the hormone concentrations observed in hospital and nursing facility wastewater. APEO concentrations in nursing home and independent living

facility wastewater were also significantly different and lower than APEOs in hospital and assisted living facility wastewater.

The dendrogram obtained from hierarchical cluster analysis is presented in Figure 2-3. This figure shows the relative similarities based on the concentration of different groups of PPCPs (pharmaceuticals, hormones and APs/APEOs) and different healthcare facility wastewater can be observed. When the concentration of pharmaceuticals was considered, the assisted living and independent living facility wastewater was found to be most similar followed by the hospital and then by the nursing care facility. For hormone concentrations, the cluster analysis revealed that the nursing care facility and the independent living facility wastewater were most similar followed by the assisted living facility and the hospital. Finally for APEOs, the nursing care facility and independent living facility were most similar in concentration, followed by the hospital and the assisted living facility. Thus, from the statistical non parametric analysis and cluster analysis it can be observed that the similarity between different healthcare facility wastewater is dependent on the group of PPCP being considered. No other correlation between the different healthcare facilities effluent concentration could be established, however, the maximum concentration within each PPCP class seemed to conceptually agree with the type of care services provided at each healthcare facility.

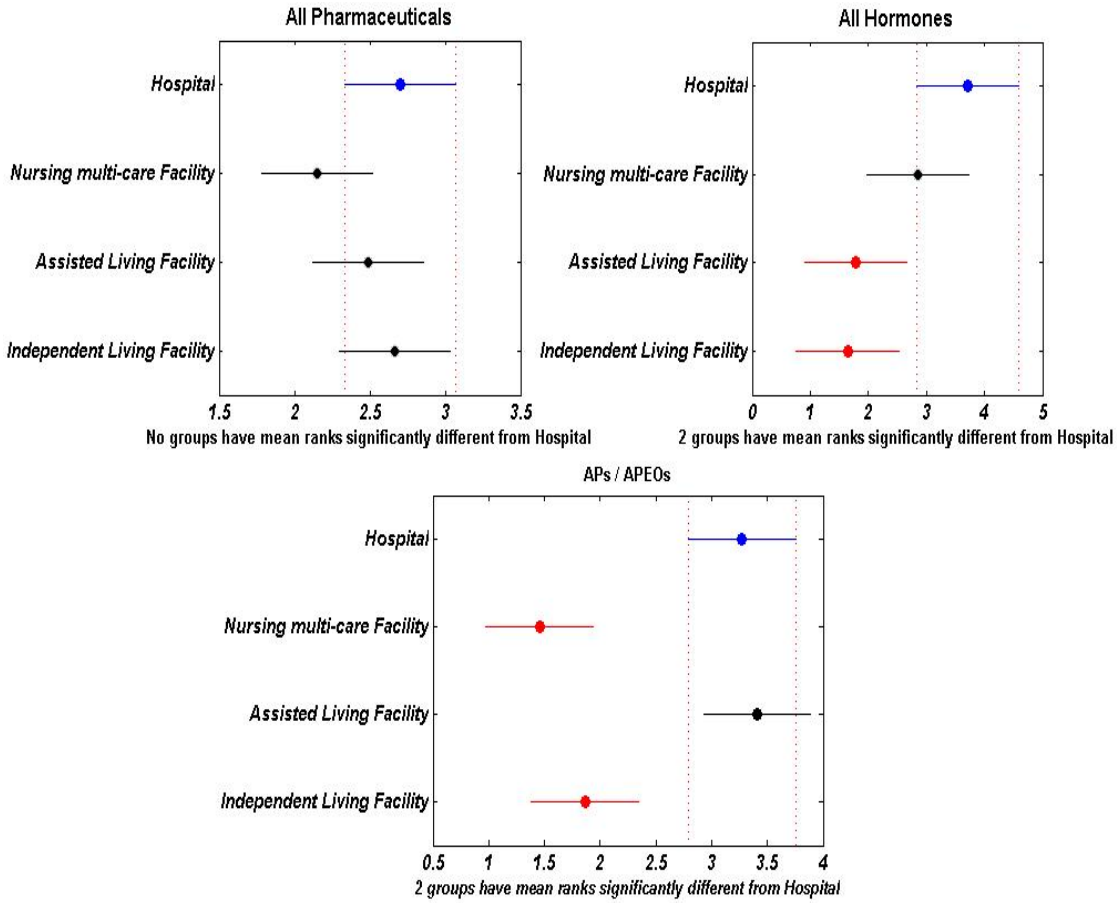


Figure 2-2 Frideman's non parametric test followed by a multiple comparison test to understand the difference between each healthcare facility's observed concentrations

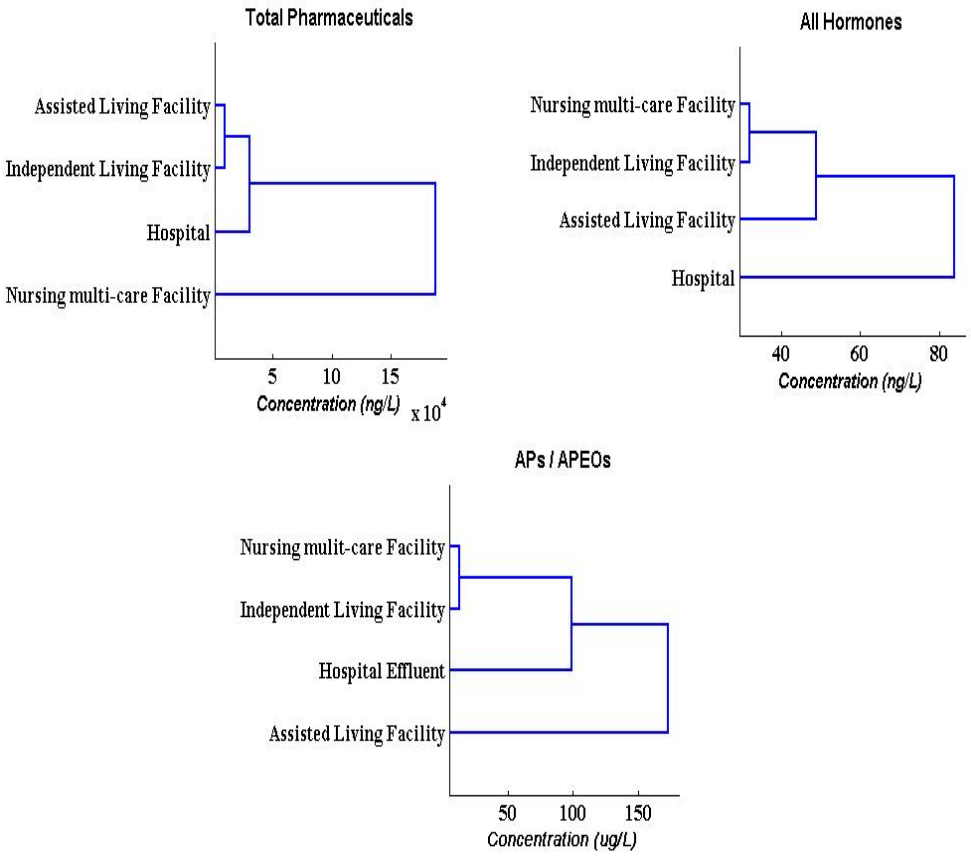


Figure 2-3 Dendrogram for sampled facilities according to the observed PPCP concentrations

2.4 Summary of Source Characterization Papers' Conclusions

Taken as a whole, the data provided within this section and within the four papers provide the most comprehensive dataset currently available for evaluating risk management options for PPCPs originating at healthcare facilities. The provided data informs risk assessment discussions by providing source characterization data for PPCPs not previously reported for hospital, nursing, assisted living, and independent living facility wastewaters. Our research provides an initial dataset for municipal officials, regulators, and healthcare facility operators that can be used to identify if risk management approaches should be implemented to reduce the release of PPCPs from healthcare facilities in their jurisdiction.

Of particular interest is the observation that the sub part-per-billion and part-per-trillion pharmaceutical and hormone analyte concentrations observed in this study are within the same order of magnitude for the same analytes reported in the literature for wastewater influents. This finding suggests that healthcare facilities are not significant sources of pharmaceuticals and hormones to municipal wastewaters when PPCPs are considered as a whole. However, the intensive use of detergents (observed by high concentration of APEOs in the effluents) in the healthcare facilities could be an important source of APs to the environment when APEO based detergents enter the municipal system and transform to APs during conveyance and treatment.

Additionally, the data indicate that the magnitude and importance of healthcare facilities as a source will vary based upon the specific PPCP of interest and the flow that the healthcare facility contributes to the municipal wastewater conveyance and treatment

system. In the municipal wastewater conveyance system sampled as part of this research, the sampled healthcare facility wastewaters only made up 0.2% of the total wastewater flow received by the municipality's treatment plant. Therefore, for risk management purposes, it is important to consider that the importance of healthcare facilities as sources of PPCPs to the municipal wastewater system will likely be most dependent upon the location of the facility in the network and the relative flow contribution of healthcare facility effluent to a municipal treatment plants total flow.

The risk of analyzed PPCPs within the environment is still a contentious issue. While the risk created by environmental exposures to pharmaceuticals is not easily quantified, the risk associated with hormones, APs, and APEOs in wastewater can be assessed (by one measure) through calculation of a samples estrogenicity. Relative potencies for hormones and APEO degradation products and the calculation for determining estrogenicity is present in the literature [66]. Based upon this metric, all of the wastewaters were estrogenic, with approximately 65% of the total estrogenicity imparted by the APEO degradation products in the samples. While the relative potency of APEO degradation products are three orders of magnitude lower than 17β-estradiol, the concentration of APEOs makes up for the difference in the relative potency. Based upon our interpretation of the data, the presence of APEOs in the sampled healthcare facility wastewaters warrant further investigation into pretreatment measures that could be used to reduce the concentration of APEOs from leaving the source.

3. ADVANCED OXIDATION OF ALKYLPHENOL ETHOXYLATES IN AQUEOUS SYSTEMS

3.1 Introduction

Alkylphenol ethoxylates (APEOs) are non-ionic surfactants commonly used to formulate products such as detergents, paints, dispersing agents, wetting products, pesticides, and petroleum recovery chemicals [71, 72]. Their widespread use in industrial and commercial formulations has resulted in the increased report of APEOs as common environmental contaminants found in surface water [48, 73, 74], groundwater [75-77] and wastewater [47, 71, 72, 78-80]. APEOs are not completely biodegradable under normal environmental conditions and result in the formation of environmentally persistent and endocrine system active alkylphenols (APs) [30, 47, 81-84]. While the estrogenic potential of APs are 3-4 orders of magnitude lower than estradiol's estrogenic activity [83, 85-87], the concentration of APEOs and APs present in environmental samples is normally three to four orders of magnitude greater than the concentration of hormones [30, 48, 75, 78, 88]. Therefore, the estrogenic potential of a water or wastewater realized when APEOs breakdown to APs can be significant. Reducing the presence of endocrine disrupting contaminants, such as nonylphenol and estrogens, from entering the environment has been a primary concern for wastewater engineers over the past decade.

Physical and chemical processes such as filtration, oxidation and advanced oxidation have been commonly used for the removal of endocrine disrupting contaminants from wastewater [77]. Removal of APs by filtration, membrane bioreactors, ozone, hydrogen peroxide, electrochemical processes and advanced oxidation techniques is reported [77, 89-92]. However, available literature exploring the treatment efficiency of different processes to degrade APEOs is currently limited. Research evaluating the degradation of APEOs is important to assess pretreatment options for facilities where APEOs are produced or extensively used, as a recent study determined that APEOs present in industrial wastewater remain practically unchanged at the source [93].

Advanced oxidation processes (AOPs) produce the hydroxyl radical (OH·), which is commonly used to eliminate organics from water and wastewater [94-96]. OH· is a highly reactive, non-selective oxidant with a high oxidation potential (2.86 eV) [97]. The effectiveness of an AOP to remove oxidize organics present in a matrix depends on the rate of OH· formation and the availability of OH· to react with the target organic compound. Effectiveness of different AOPs for oxidation of different micro contaminants in the environment is well documented in literature [20, 95, 96]. However, oxidation of APEOs using AOPs has not previously been explored to the best of our knowledge.

Research was performed to explore the oxidation of APEOs by AOPs in ultrapure water and in aqueous environmental matrices. Three AOPs were explored to determine the ability of each AOP to degrade APEOs in aqueous systems. The AOPs

studied were hydrogen peroxide in the presence of ultraviolet light (UV/H_2O_2), Fenton's reagent (Fe/H_2O_2), and photo-Fenton's ($UV/Fe/H_2O_2$). The purpose of this research was to understand the reaction kinetics of APEOs in the presence of OH·, monitor any observed degradation products, and to use APEO removal data within AOP systems to evaluate a predictive model for the removal of APEO in aqueous environmental matrices based upon OH· formation rate and OH· scavenging rate constant. This predictive model has important implications for evaluating the effectiveness of AOPs as treatment or pretreatment technologies for removal of APEOs within municipal and industrial wastewater systems.

3.2 Experimental Section

3.2.1 Chemicals and reagents

ACS grade phosphoric acid, phosphate buffer, tertiary butanol, parachlorobenzoic acid, HPLC grade acetonitrile and water, H_2O_2, ferric sulfate, and glacial acetic acid were purchased from Fisher Scientific (Pittsburg, PA). Ultrapure water was produced in the laboratory using a Barnstead NANOpure water unit. UV light was generated using a 254 nm UV lamp contained in a boxed enclosure in order to keep out residual light and for safety purposes.

Triton-X 100™ and Tergitol 15™ were purchased from Dow Chemical (Midland, MI). Triton-X 100™ is a mixture of octylphenol ethoxylates (OPEOs) with an average ethoxylate chain length of 10. Tergitol 15™ is a mixture of nonylphenol ethoxylates (NPEOs) with an average chain length of 15. Spiking solutions of OPEO

and NPEO were prepared by diluting 20 g/L stock solutions of the two APEOs using ultrapure water. The 20 g/L stock solutions were created by dissolving neat compound as received from Dow in ultrapure water at 40 ^{o}C while stirring. Stock and spike solutions were immediately used upon creation.

3.2.2 Experimental setup

Oxidation of OPEO and NPEO was explored using three AOP systems including UV/H_2O_2 (UH), Fe/H_2O_2 (FH), and UV/Fe/H_2O_2 (UFH). Reactions were carried out in triplicate within 2 L glass beakers to evaluate each process. 1 L of aqueous sample was placed in each beaker and spiked with either OPEO or NPEO at a concentration of 5 μM. Reaction systems that involve UV irradiation were carried out by placing individual reactors within the boxed UV enclosure. The reactors inside the enclosure were placed on a multiposition stir plate and the surface of the reactor solution was 12.5 cm from the UV source.

OH· reaction kinetics with the two APEOs was studied by measuring the degradation of OPEO and NPEO in the UH system in ultrapure water with a H_2O_2 concentration of 0.6 mM. The rate constant for the reaction of OPEO and NPEO with OH· was determined through competition kinetics with methylene blue as the reference compound. The rate of OH· formation from each AOP and the OH· scavenging rate constant for each aqueous environmental matrix were calculated.

3.2.3 Analytical measurements

Samples from the oxidation reactions in laboratory ultrapure water and four aqueous environmental matrices were analyzed for APEOs, dissolved organic carbon content (DOC), and dissolved ozone and were screened for the formation of degradation products. The four aqueous environmental matrices used in this study were collected in 10 L volumes. The sources of the samples were potable water, a wastewater effluent conveyance channel, a wastewater influent main, and an effluent main from a municipal hospital. All samples were collected into polypropylene bottles using a peristaltic pump with teflonated tubing and were immediately placed on ice and returned to the laboratory for testing. Prior to their use in the semi-batch reactor system, the aqueous environmental matrices were filtered through a 1 μm glass fiber filter.

3.2.4 APEO analysis

Extraction and analysis of APEOs was performed at US EPA Region 5's Central Research Laboratory (R5CRL) according to US EPA R5CRL's standard operating procedure MS006 V1. Reaction solutions (1 L) received 3 mL of methanol and 1 mL of formaldehyde to preserve the samples and were shipped overnight to R5CRL in 1 L amber glass bottles packed on ice. The full method is described in a previous publication [66]. Briefly, 1L of filtered sample (0.45 μm) was analyzed using a Waters 2659 liquid chromatography coupled with a single quadrapole ZQ mass spectrometer. The analytes were separated using an Atlantis ™ MS C_{18} column (150 mm x 2.1 mm x 3 μm). The target analytes were quantified using a single ion recording (SIR) operated under atmospheric electrospray positive ion mode. The details about the

instrumentation, method detection limits and quality control protocol is reported within the CRL's SOP. A five point calibration curve was used to quantify total NPEO and total OPEO based upon the primary ion response for NPEOs with an ethoxylate chain length between 3 and 18 and OPEOs with an ethoxylate chain length between 2 and 12. The secondary ion response of each individual NPEO and OPEO was used for verification. Analyte recovery was assessed through matrix spiked additions of OPEO and NPEO at a concentration of 100 ppb. The acceptable range of recovery used in the analysis and reporting of experimental data was 60% to 140%.

3.2.5 Measuring para-chlorobenzoic acid in solution

Para-chlorobenzoic acid (p-CBA) is used in experiments to determine the ratio of OH· formation for individual AOPs and OH· scavenging rate constant for each matrix. The concentration of p-CBA in reaction solutions is measured using a UV spectrophotometer operated at 235 nm using a six point external calibration curve.

3.2.6 Total organic carbon

Total dissolved organic carbon was analyzed using a Shimadzu 6000V TOC Analyzer according to Standard Method 5310B [98].

3.3 Results and Discussion

3.3.1 Reaction kinetics and degradation products formed during the reaction of APEOs with OH·

The reaction kinetics and degradation products of the reaction of APEOs with OH· were evaluated in ultrapure water using the UH system. Because the reaction rate constant for the reaction of APEO with OH· is expected to be in the range of 10^7-10^{11} $M^{-1}s^{-1}$, the second-order rate constant determined in this research was calculated using competition kinetics ([99-104]). The application of the competition kinetics model in our experimental system leads to the following relationship described in equation (3-1).

$$\ln\left(\frac{[APEO]}{[APEO]_0}\right) = \frac{k_{OH-APEO}}{k_{OH-R}} \ln\left(\frac{[R]}{[R]_0}\right) \quad 3\text{-}1$$

where $[APEO]_0$ and $[R]_0$ are the initial concentration of APEO and the reference compound (methylene blue) at time = 0, k_{OH-R} is the rate constant for the reference compound ($4.1x10^9$ $M^{-1}s^{-1}$), $k_{OH-APEO}$ is the second-order rate constant for the reaction of APEO with OH·, and [APEO] and [R] are the concentrations of APEO and the reference compound at time = t. The slope obtained by plotting $\ln\left(\frac{[APEO]}{[APEO]_0}\right)$ versus $\ln\left(\frac{[R]}{[R]_0}\right)$ was used to determine the second-order rate constant. The second-order rate constant for NPEO and OPEO were both determined to be $1.1x10^{10}$ $M^{-1}s^{-1}$. These rate constants are similar to the 10^7 to 10^{11} range of second-order rate constants for the reaction of organics with OH· presented in the literature [95, 96, 101, 105].

Figures 3-1 and 3-2 present a time series evaluation of the reaction products that clearly indicates the formation of shorter chain length ethoxylates during chemical

reaction. Reaction products observed in the reaction solutions that were not present in the initial spiked solution include OP_3EO for the OPEO investigation and NP_2EO, and NP_3EO for the NPEO investigation. Therefore, fragmentation of the ethoxylate chain length does occur during advanced oxidation of APEOs. However, the overall concentration of all ethoxylate chain lengths decreases at each time step from an initial concentration of 5 μM down to 0.05 μM after fifteen minutes. While a slight increase in the concentration of lower APEOs was observed over time, the data does not distinguish whether the observed lower ethoxylates formed due to progressive fragmentation of the ethoxylate chain length or from the non-selective attack of OH· at various parts of the molecule.

While the fast rate of reaction between OH· and APEOs indicates that treatment of APEOs in aqueous environmental matrices using advanced oxidation processes is favorable, the resulting oxidation of APEOs by individual AOPs will be dependent upon aqueous environmental matrix used in experimental system.

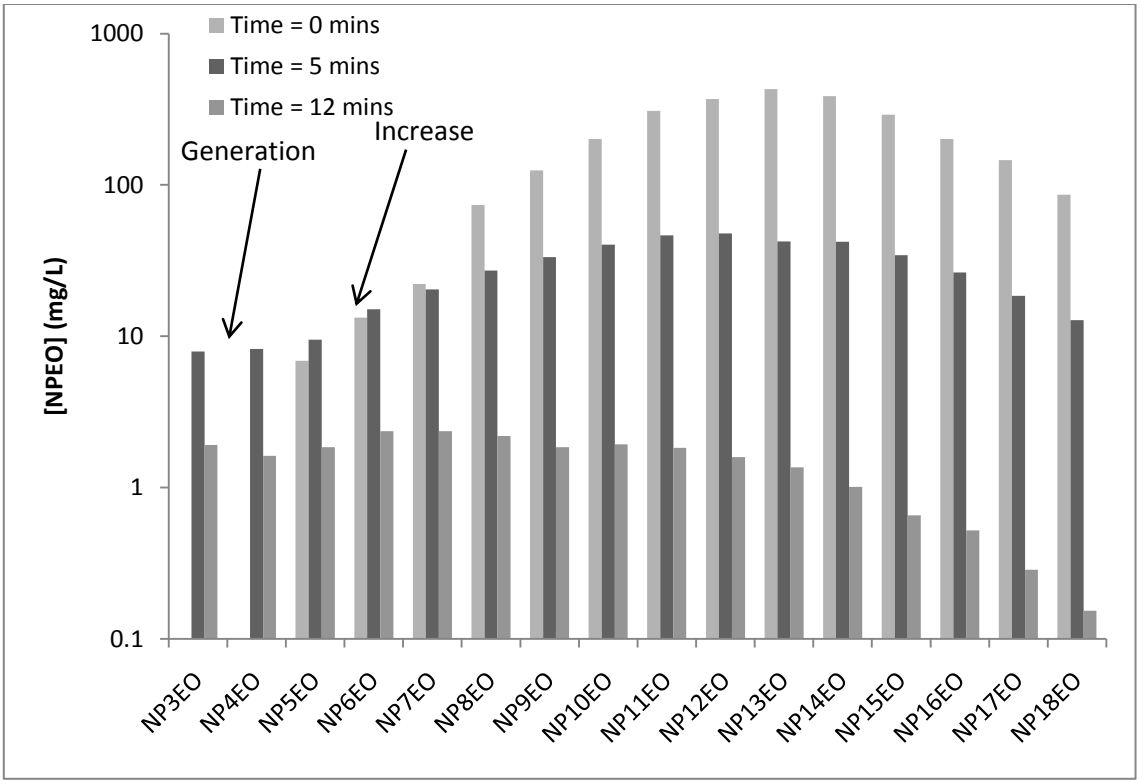


Figure 3-1 Concentration of individual nonylphenol ethoxylates (NPEOs) measured during the reaction of NPEOs with hydroxyl radical in ultrapure water within the UV/H2O2 system after five and twelve minutes of reaction

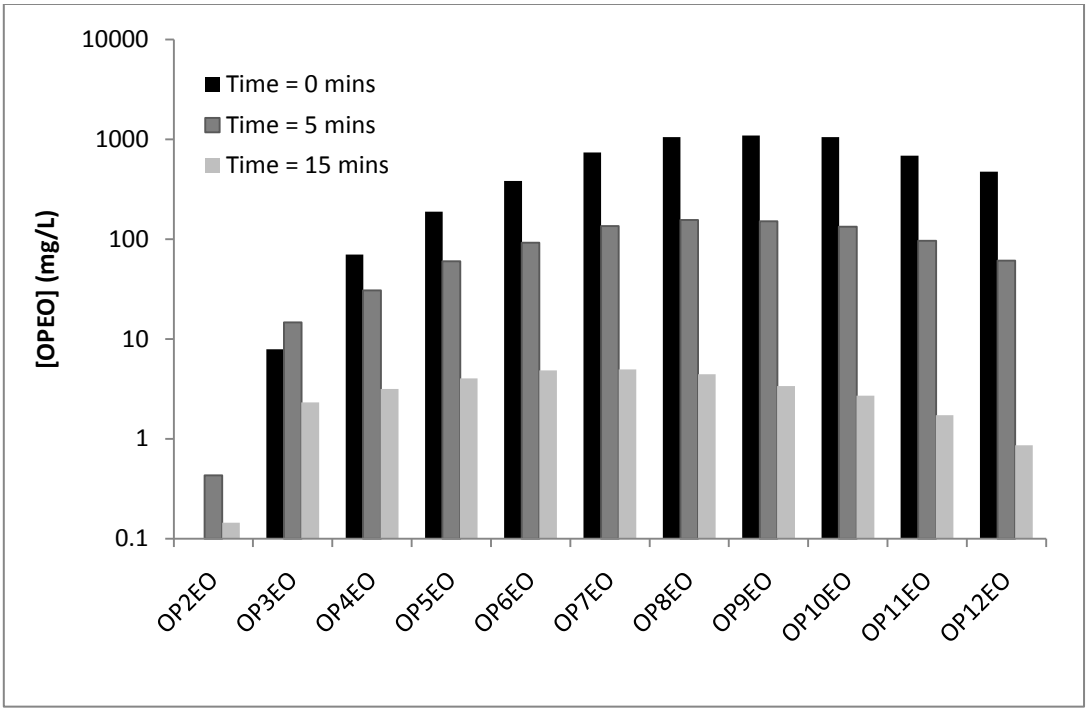


Figure 3-2 Concentrations of individual octylphenol ethoxylates (OPEOs) measured during the reaction of OPEOs with hydroxyl radical in ultrapure water within the UV/H2O2 system after five and twelve minutes of reaction

3.3.2 Oxidation of APEOs in different aqueous matrices

The impact of different aqueous environmental matrices on APEO oxidation by each evaluated AOP reaction system was also evaluated. Table 3-1 shows the experimental conditions and the resulting APEO removal after ten minutes of reaction for each AOP – matrix pair. APEO removal was greatest in tap water followed by wastewater effluent, wastewater influent, and hospital effluent in respective order. This observation is intuitive as less oxidant is available for oxidation of the APEOs when higher amounts of DOC are present to scavenge OH·. Therefore, the difference in the APEO removal for each matrix-AOP pair can be explained based on the OH· formation rate and scavenging rate constant.

3.3.3 Determining OH· formation rate and scavenging rate constant in matrix-AOP pairs

The oxidation of an organic target compound [P] with OH· depends on the second-order rate constant of the target compound, the rate of OH· formation from each AOPs and the OH· scavenging rate constant of the matrix. The rate of target compound oxidation in a batch reactor d[P]/dt by OH· follows pseudo first-order reaction kinetics described by Equation (3-2) [106].

$$-\frac{d[P]}{dt} = k_{expt}\,[P] \qquad 3\text{-}2$$

where [P] is the concentration of target analyte in solution and k_{expt} is the pseudo first-order rate constant which is function of OH· formation rate and scavenging rate constant.

Table 3-1 Percent removal of APEOs in environmental aqueous matrices after ten minutes of reaction for each matrix - AOP reaction pair

AOP	Aqueous Matrix	H_2O_2 μM	Fe μM	UV	OPEO % removal	NPEO %removal
UH	Ultrapure water	600	-	254 nm	97.1	97.1
UH	Tap water	600	-	254 nm	76.4	73.5
UH	WWTP effluent	600	-	254 nm	53.0	62.2
UH	WWTP influent	600	-	254 nm	14.8	8.5
UH	Hospital effluent	600	-	254 nm	11.8	3.1
FH	Ultrapure water	100	25	-	85.8	82.2
FH	Tap water	100	25	-	63.4	67.6
FH	WWTP effluent	100	25	-	26.7	27.7
FH	WWTP influent	100	25	-	5.2	8.9
FH	Hospital effluent	100	25	-	3.8	0.6
UFH	Ultrapure water	100	25	254 nm	95.5	94.4
UFH	Tap water	100	25	254 nm	60.5	63.9
UFH	WWTP effluent	100	25	254 nm	23.9	34.7
UFH	WWTP influent	100	25	254 nm	17.4	24.7
UFH	Hospital effluent	100	25	254 nm	12.5	12.1

Determination of OH· formation and scavenging rate constant is accomplished by measuring the removal of para-chlorobenzoic acid (p-CBA, a commonly used probe compound) spiked into solution in the presence of tertiary butanol (t-BuOH, a known OH· scavenger) in each matrix-AOP pair. The initial concentration of p-CBA in solution is kept constant at 5 μM while the initial concentrations of t-BuOH are varied from 50, 100, 200, 600, and 1000 μM in each matrix – AOP pair. The decrease in the p-CBA concentration in these experiments also follows the pseudo first-order kinetics as described in equation 3-3. For each matrix-AOP pair, five k_{expt} value are calculated from the slope of the concentration time profile of p-CBA for five different t-BuOH initial concentrations using Equation (3-3).

$$-\ln\left(\frac{[pCBA]}{[pCBA]_0}\right) = k_{expt}t \qquad 3\text{-}3$$

Figure 3-3 shows the plot between $\ln\left(\frac{[pCBA]}{[pCBA]_0}\right)$ and time for the tap water–UH pair. k_{expt} is also further defined in Equation (3-4) as:

$$k_{expt} = k_{OH-pCBA}\,\psi \qquad 3\text{-}4$$

Where $k_{OH-pCBA}$ is a second-order rate constant known from literature and ψ is the ratio between OH· formation rate and scavenging rate constant within each matrix-AOP pair. ψ is described mathematically by Equation 3-5

$$\psi = \frac{OH\cdot\ formation\ rate}{OH\cdot\ Scavenging\ rate\ constant}$$

$$= \frac{\phi}{k_{OH-H_2O_2}[H_2O_2] + k_{OH-HCO_3}[HCO_3^-] + k_{OH-DOC}[DOC] + k_{OH-tBuOH}[tBuOH]}$$

3-5

The components of the OH· scavenging rate constant are known or found experimentally. Under the given experimental conditions, DOC, bicarbonate/carbonate ion, H_2O_2 and tBuOH are the predominant OH· scavengers species present in the different water matrices.

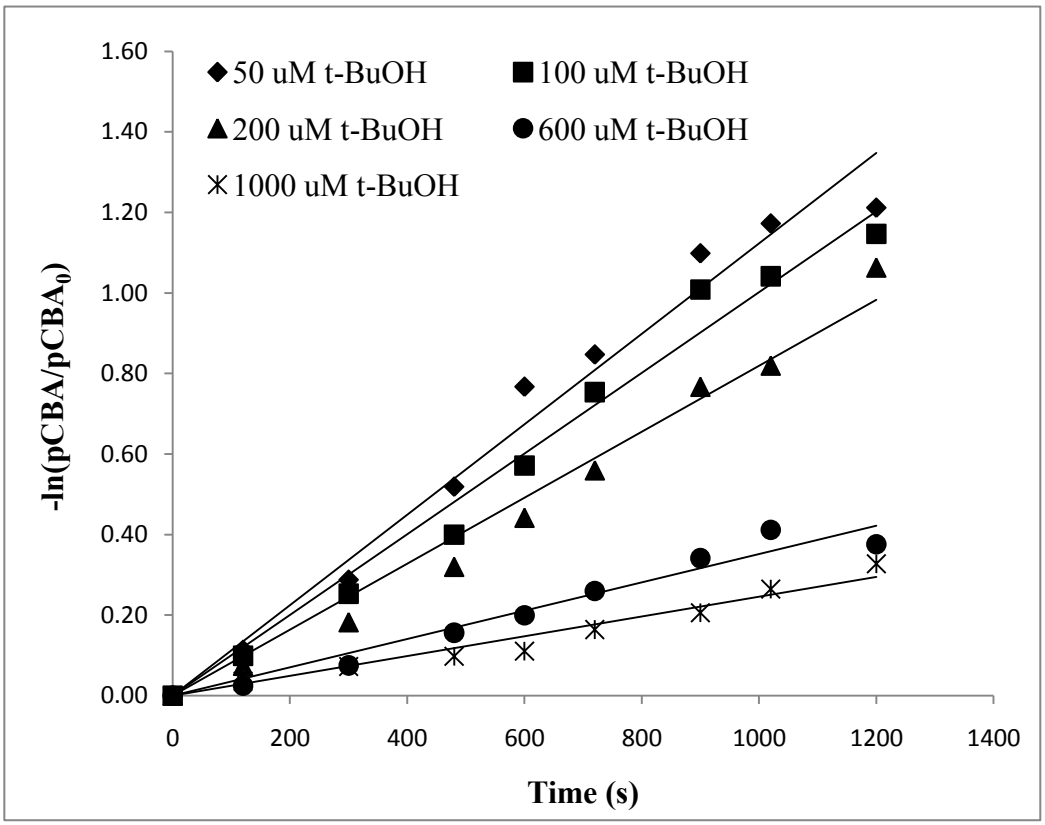


Figure 3-3 Degradation of p-CBA in tap water during the reaction with OH· and p-CBA within the UV/H2O2 system. The value of kexpt is calculated for five t-BuOH concentrations

Substituting Equation (3-5) into Equation (3-4) results in Equation 3-6.

.

$$k_{expt} = k_{OH-pCBA} \frac{\phi}{k_{OH-H_2O_2}[H_2O_2]+k_{OH-HCO_3}[HCO_3^-]+k_{OH-DOC}[DOC] + k_{OH-tBuOH}[tBuOH]} \quad 3\text{-}6$$

Taking the inverse of Equation (3-6) and separating out terms results in Equation (3-7).

$$\frac{1}{k_{expt}} = \frac{k_{OH-H_2O_2}[H_2O_2]+k_{OH-HCO_3}[HCO_3^-]+k_{OH-DOC}[DOC]}{k_{OH-pCBA}\,\phi} + \frac{k_{OH-tBuOH}}{k_{OH-pCBA}\,\phi}[tBuOH] \quad 3\text{-}7$$

Figure 3-4 shows a linear plot of Equation (3-7) where $\frac{1}{k_{expt}}$ is plotted versus tBuOH concentration for one of the matrix–AOP pairs (tap water-UH). The slope of this graph is used to calculate OH· formation rate ϕ and the y-intercept is used to determine the value of k_{OH-DOC}. ϕ and k_{OH-DOC} were calculated for each matrix-AOP pair using this methodology. The resulting OH· formation rate ϕ for a given AOP and the k_{OH-DOC} for each matrix are presented in Table 3-2. k_{OH-DOC} values presented in Table 3-2 are within the range of reported k_{OH-DOC} values (1.4 – 8.6 x 10^4 L mg^{-1} s^{-1}) for different wastewater effluents reported in the literature [106, 107].

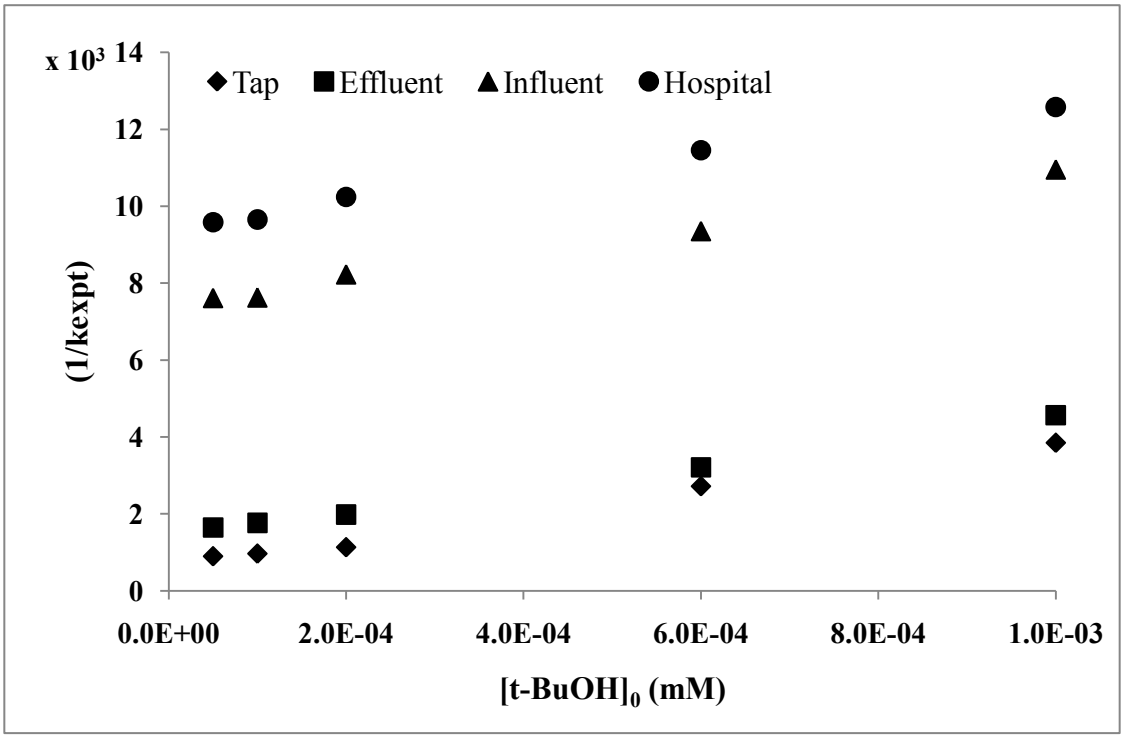


Figure 3-4 Plot of 1/kexpt found from equation 3-3 versus t-BuOH concentration for the UV/H2O2 system and all water matrices

Table 3-2 Hydroxyl radical formation rate (ϕ) for each AOP and second-order kinetic constant for DOC ($k_{OH\text{-}DOC}$) of each environmental water matrix used in this study with additional measured water quality parameters

Water	[DOC]	$[HCO_3^- / CO_3^{2+}]$	k_{OH-DOC}	ϕ_{UH}	ϕ_{FH}	ϕ_{UFH}
	mg C/L	M	L mg^{-1} s^{-1} ($x10^{-3}$)	M s^{-1} ($x10^{8}$)	M s^{-1} ($x10^{8}$)	M s^{-1} ($x10^{8}$)
Tap Water	0.71	8.92E-03	7.14 (±0.75)	3.49 (±0.18)	1.51 (±0.10)	2.86 (±0.32)
WWTP Effluent	3.54	7.67E-03	48.41 (±1.61)			
WWTP Influent	22.14	6.83E-03	57.31 (±8.14)			
Hospital effluent	27.38	5.58E-03	60.69 (±1.76)			

ϕ - Hydroxyl radical formation rate, UH – UV/H_2O_2, FH – Fe/H_2O_2, UFH – $Fe/UV/H_2O_2$

The total scavenging rate constant for each matrix were calculated to be $1.0x10^5$ s^{-1} for tap, $2.6x10^5$ s^{-1} for WWTP effluent, $15x10^5$ s^{-1} for WWTP influent and $17x10^5$ s^{-1} for hospital effluent. The OH· scavenging rate constant for natural water systems have been reported as $3x10^4$ s^{-1} for low DOC lake water to $3x10^5$ s^{-1} for secondary effluents following treatment [107]. The OH· scavenging rate constant is dependent on the concentration of total dissolved organic matter and the concentrations of inorganic scavenger compounds present in water. This explains why the highest OH· scavenging rate constant calculated in our studies was for the hospital effluent and the WWTP influent. Also, while tap water had the highest concentration of HCO_3^-/CO_3^{2-} ($9x10^{-3}$ M), it also had the lowest concentration of dissolved organic matter (0.7 mgC L^{-1}). As a result the total OH· scavenging rate constant for tap water was lowest in comparison to the other aqueous environmental matrices.

In addition to the OH· scavenging rate constant, the rate of OH· formation (ϕ) was also calculated from the above equations. The OH· formation rate did not change with the different water matrices, however differences in radical formation based upon the individual AOP was observed.

3.3.4 APEO percent removal in matrix-AOP pairs

Within our experimental system the extent of observed APEO removal within each matrix-AOP pair was dependent directly on the OH· formation rate and inversely dependent on OH· scavenging rate constant of the water matrix. In order to access this dependency, APEO concentrations for each matrix – AOP pair were predicted after 10

minutes of reaction by modifying the modeling approach presented in section 3.3 to account for APEO as a target compound. Equation (8) is the modified equation.

$$[APEO]_t = [APEO]_0 \times \exp\left(-\frac{k_{OH-APEO}\cdot\phi\cdot t}{k_{OH-H_2O_2}[H_2O_2]+k_{OH-HCO_3}[HCO_3^-]+k_{OH-DOC}[DOC]+k_{OH-MeB}[MeB]}\right) \quad 3\text{-}8$$

The OH· scavenging rate constant of different water matrices, the OH· formation rate within different AOPs, and the kinetic rate constants listed in Tables 3-2 and 3-3 were used in Equation (8) to predict the concentration of APEO in reactor solutions after ten minutes. Table 3-4 presents the predicted and observed APEO concentration.

Table 3-3 Kinetic rate constants utilized in the presented modeling approach

	Constant	Units	Reference
$k_{OH-pCBA}$	5.30E+09	$M^{-1}s^{-1}$	[107]
k_{OH-MeB}	4.14E+09	$M^{-1}s^{-1}$	This Study
$k_{OH-OPEO}$	1.07E+10	$M^{-1}s^{-1}$	This study
$k_{OH-NPEO}$	1.12E+10	$M^{-1}s^{-1}$	This Study
$k_{OH-HCO_3^-}$	1.10E+07	$M^{-1}s^{-1}$	[107]
$k_{OH-H_2O_2}$	2.70E+07	$M^{-1}s^{-1}$	[107]
$k_{OH-tBuOH}$	6.00E+08	$M^{-1}s^{-1}$	[107]

Table 3-4 Final concentration of predicted and observed values of APEOs in ultrapure water, tap water, WWTP effluent, WWTP influent and hospital effluent for each AOP

AOP	Aqueous Matrix	$[OPEO]_t$		$[NPEO]_t$	
		observed μg/L	predicted μg/L	observed μg/L	predicted μg/L
UH	Ultrapure Water	22.3	0.66	433	112
UH	Ultrapure Water	32.5	0.66	77.4	4.76
UH	Ultrapure Water	930	279	142	23.13
UH	Ultrapure Water	168	13.5	23.5	1.34
UH	Tap Water	678	433	353	188
UH	Wastewater Effluent	1350	1240	504	565
UH	Wastewater Influent	2450	2390	1220	1120
UH	Hospital Effluent	2530	2480	1290	1160
FH	Ultrapure Water	816	91.7	473	35.2
FH	Tap Water	1050	1130	431	512
FH	Wastewater Effluent	2100	1940	964	901
FH	Wastewater Influent	2720	2620	1210	1240
FH	Hospital Effluent	2760	2660	1330	1260
UFH	Ultrapure Water	260	2.27	150	1.05
UFH	Tap Water	1130	498	481	236
UFH	Wastewater Effluent	2190	1390	870	656
UFH	Wastewater Influent	2370	2460	1000	1160
UFH	Hospital Effluent	2510	2530	1170	1200

Predicted and observed [APEO] concentrations are used to calculated fractional removal $\left(1-\frac{[APEO]_t}{[APEO]_0}\right)$. Figure 3-4 represents the predicted versus observed fractional removal of APEOs and the residual plot when the data is fitted to a linear equation with slope equal to one and an intercept equal to zero using a linear squared method. The summary of goodness of fit analysis of the model is presented in Table 3-5.

The data presented in Figure 3-5 was further evaluated by considering two groups of data. Group 1 consisted of all data with fractional removals less than 0.5 and Group 2 consisted of all data with fractional removals greater than 0.5 (group 2). The average residuals for Group 1 data (0.06) were lower than the average residuals for Group 2 data (0.11). A further exploration of the data reveals that Group 2 corresponds to the experiments carried out in ultrapure water, tap water and wastewater treatment plant effluent while Group 1 data corresponds to experiments conducted with wastewater treatment plant influent and hospital effluent. These findings suggest that there is greater deviation within the predicted values from the experimental values for Group 2 data points when compared with Group 1 data points.

The observed difference can be explained due to the basic model assumption that the concentration of the all the scavenging species within the water matrix does not change with reaction progression. However, with the ultrapure water this assumption cannot be true due to an overall lack of $OH^{\cdot}$ scavenging species. This explanation can also be extended to tap water and WWTP effluent due to low concentrations of dissolved organic carbon observed in those samples. Therefore, before implementing AOPs as a treatment / pretreatment technology for removal of APEOs with different water matrices,

it is important to understand the rate of hydroxyl radical formation along with the scavenging capacity of water.

Table 3-5 Goodness of fit statistics for fitted predicted fractional removal of APEOs with a linear polynomial with slope as one and y-intercept as zero

Fittedmodel	
Linear model Poly1:	Fittedmodel1(x)=p1*x + p2 Coefficients (with 95% confidence bounds): p1 = 1 (fixed at bound) p2 = 0 (fixed at bound)
SSE	0.585
R^2	0.884
DF	36
Adjusted R^2	0.887
RMSE	0.127

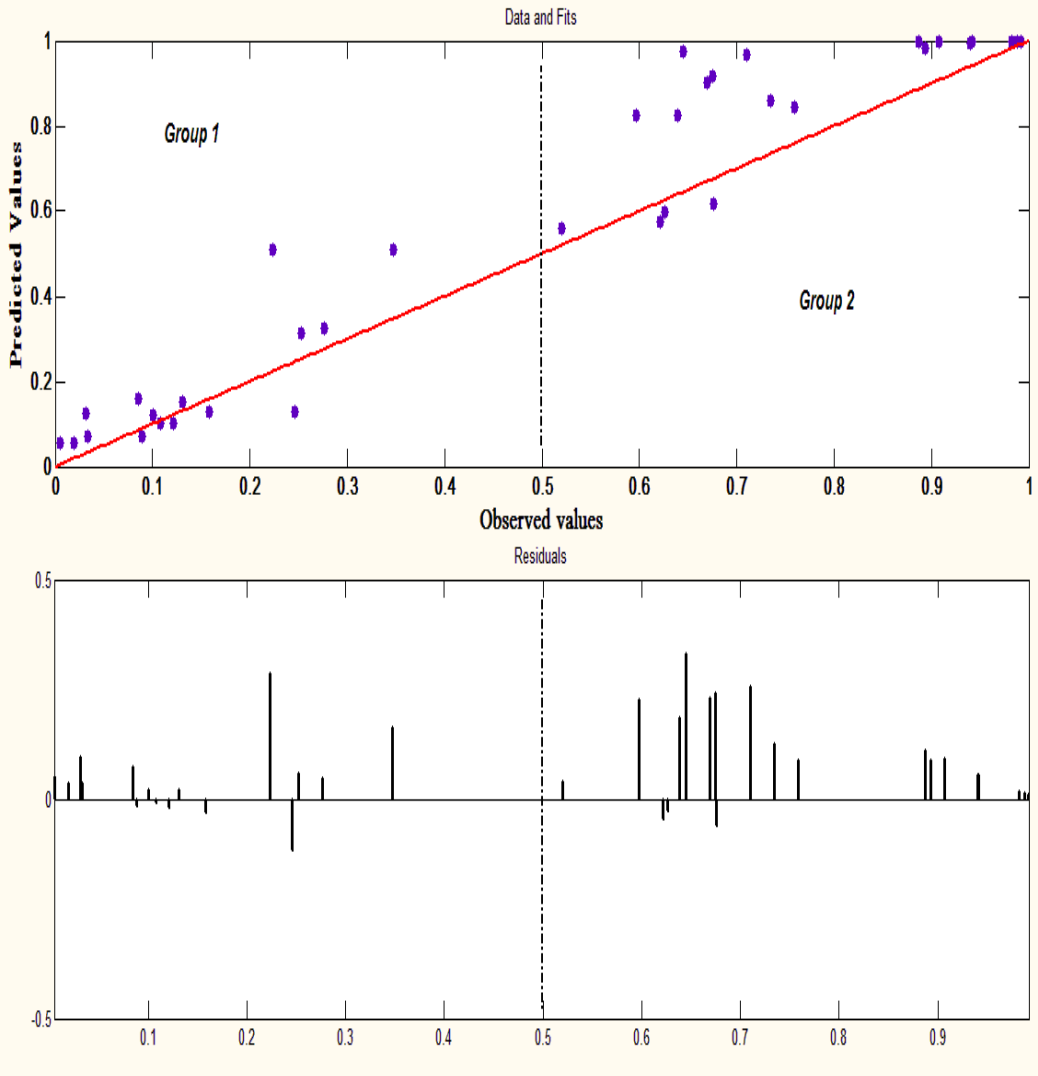


Figure 3-5 Plots of predicted versus observed values of fractional removal of APEO for all the performed experiments. Trends in the data are observed when separating the plot into two respective groups. Group 1 has predicted removals less than 50% and corresponds to the hospital effluent and wastewater influent samples and Group 2 has predicted – observed removals greater than 50% corresponding to ultrapure water, tap water, and wastewater effluent samples.

3.3.5 Implications for using AOPs to treat APEOs in wastewater

The reaction of APEOs with OH· in ultrapure water and aqueous environmental matrices followed second-order reaction kinetics with a calculated rate constant for both APEOs of $1.1x10^{10}$ $M^{-1}s^{-1}$. During the reaction of APEOs with OH·, APEOs with lower ethoxylate chain length were formed, indicating fragmentation. While formation of APEOs with smaller ethoxylate chains was observed, the concentration of all APEOs decreased rapidly in solution.

Removal of APEOs was observed in all aqueous environmental matrices by all of the evaluated AOPs. The differences in the percent removal of APEOs for each water matrix–AOP pair can be explained by the rate of OH· formation, which is affected by the oxidant used by each AOP, and by the rate of OH· scavenging, which is affected by concentrations of scavenging chemicals in the aqueous environmental matrix. Predictions of fractional removal of APEO within each matrix-AOP pair describe the experimental data well (r^2 of 0.88). The presented modeling approach can also be used to design an advanced oxidation process to remove APEOs from aqueous systems by utilizing the model to estimate the dosages of oxidant based upon the time required to achieve desired removal of APEOs. Therefore, the presented approach can be used by municipalities and design engineers to assess the location for implementing treatment within a wastewater conveyance system or treatment system based on the technical and economic feasibility.

4. MOLECULAR OZONATION OF ALKYLPHENOL ETHOXYLATES IN AQUEOUS SYSTEMS

4.1 Introduction

Alkylphenol ethoxylates (APEOs) are an important class of non-ionic surfactants [71, 72]. Due to their widespread use in industrial processes and consumer products, APEOs are released to wastewater [47, 71, 72, 78-80]. Concern over the presence of APEOs in wastewater arises from the observation that APEOs degrade into alkylphenols (APs) during biological processes occurring in municipal wastewater conveyance and treatment systems [48, 81, 83]. The presence of APs in wastewater is problematic because APs are recognized endocrine disrupting compounds (EDCs) that contribute to the observed estrogenicity of treated wastewater effluents [30, 47, 81-84]. Therefore, evaluating treatment technologies that can remove APEOs, APs, and other EDCs from wastewater is one of the most current and important challenges facing wastewater engineering research.

Recently, our research group evaluated the ability of advanced oxidation processes to treat APEOs present in water and wastewater (Section 3). While APEOs were degraded due reaction with hydroxide radicals, low levels of shorter chain APEO degradation products were observed during the reaction. While the ability to remove APEOs through advanced oxidation processes is evident, an interest in oxidation systems with the selective capability to eliminate the APEO phenolic ring without

forming shorter chained APEO degradation products during the reaction process is desirable as the phenolic ring is responsible for the ability of the compound to disrupt endocrine systems [38, 85, 86, 108].

Ozone is a well known and powerful oxidant (E^0 = 2.08 V) commonly used in treatment process applications to remove organics from water and wastewater [62, 102, 109-111]. While the treatment of organics with ozone at high solution pH (pH>9) leads to the formation of hydroxide radicals that dominate the oxidation mechanism, ozonation at neutral and acidic pH fosters the formation of molecular ozone that has demonstrated specificity for reacting with double bonds within aromatic rings [103, 112]. The use of molecular ozone has proven effective for removing micropollutants from wastewater [100, 101, 103, 104, 113, 114] and has been previously investigated for the oxidation of APs and phenols from water and wastewater [105]. However, oxidation of APEOs in the presence of molecular ozone has not previously been explored.

Research was carried out to assess the ability of molecular ozone to degrade APEOs from aqueous matrices through selective reactivity with the phenolic portion of the molecule. This chapter presents the kinetic rate constants for the reaction of nonylphenol ethoxylate (with an average ethoxylate chain length of 15) and octylphenol ethoxylate (with an average chain length of 10) with molecular ozone in batch and semi–batch reactors. The aims of the experiments presented in this research were to determine the effectiveness of molecular ozone in oxidizing APEOs; to determine the second-order rate constants for the reaction between molecular ozone and NPEO or OPEO; to understand the impact of different aqueous environmental matrices on the rate constant

and removal efficiency of APEOs; to understand the effect of the ethoxylate group chain length on the kinetic rate constant; and to determine the mechanism of molecular ozone reaction with APEOs. The resulting data has important implications for using ozone as a treatment technology to remove APEOs from municipal or industrial wastewater.

4.2 Experimental Section

4.2.1 Chemicals and reagents

Triton-X 100™ (an OPEO mixture with a mean ethoxylate chain length of 10) and Tergitol 15™ (a NPEO mixture with a mean chain length of 15) were purchased through Dow Chemical (Midland, MI, USA). A Barnstead NANOpure water unit was used to produce the ultrapure water used in the oxidation experiments. Acetonitrile (HPLC grade), glacial acetic acid, phosphoric acid, phosphate buffer and *tert*-butanol were purchased from Fisher Scientific (Pittsburg, PA, USA). Nonylphenol (NP) and octylphenol (OP) were purchased from Sigma Aldrich

20 g/L stock solutions of OPEO and NPEO were prepared by dissolving neat compound in ultrapure water at 40 ^{o}C with continuous stirring. Stock solutions were stored covered at room temperature and were immediately used. Small aliquots (spikes) of OPEO and NPEO were directly added to the batch or semi-batch reactor system to achieve the desired APEO concentration in the reactor. For the batch reactor system, 18 ppm ozone stock solution was prepared by dissolving ozone produced by the ozone generator in ultrapure water that was acidified to pH 3 using phosphoric acid. All ozone stock solutions were prepared in an ice bath. [104, 115]. Ozone was generated for batch

and semi-batch reactor experiments using pure industrial grade oxygen connected to a TG-10 Ozone Solutions (Hull, IA) ozone generator.

4.2.2 Experimental system description

Experiments were carried out at ambient temperature (22 °C) using triplicate 2-L glass beakers that were continuously stirred. The batch reactor system, used to study reaction kinetics and degradation product formation in ultrapure water, consisted of 1L of pH-buffered (pH of 3 or 6) ultrapure water with an initial ozone concentration of 0.4 ppm. The pH was buffered using phosphoric acid and/or phosphate buffer. *Tert*-butanol was also added to the batch reactor at a concentration of 10 μM to serve as a hydroxyl radical ($OH^{\cdot}$) scavenger [104, 115] during the experiments. The ozone concentration was monitored using an ozone probe and the self-degradation of ozone was monitored until the dissolved ozone concentration within the batch reactor reached 0.3 ppm (6.25 μM). Once the ozone concentration reached 0.3 ppm, a spiked aliquot of OPEO or NPEO was then added to the batch reactor to achieve a reactor concentration of 62.5 μM (ten times the ozone concentration) to begin the experimental run. This amount of APEO was provided in excess to determine the pseudo first-order reaction constant for ozone consumption kinetics. Ozone was continuously monitored and the decrease in ozone concentration was recorded every five seconds for the duration of the experiment to determine the kinetic rate constants.

The semi-batch reactor system, used to determine reaction kinetic constants and to evaluate the impact of the matrix, consisted of 1L of ultrapure water or aqueous environmental matrix with a spiked OPEO or NPEO concentration of 20 μM. Ozone

was then bubbled into the system at a constant concentration and flow rate using a gas diffuser stone. Ozone was continuously monitored and the ozone concentration was recorded every 30 seconds for the duration of the experiment. Semi-batch experiments were sampled over five intervals to determine the concentration of OPEO and NPEO in the reactor as a function of time for both ultrapure water and the aqueous environmental matrices.

4.2.3 Analytical methods

Descriptions of many of the analytical methods used in this research appear in a previous publication [66]. Briefly, samples resulting from the reaction of molecular ozone with the two APEOs in ultrapure water or in aqueous environmental matrices were analyzed for the concentration of dissolved organic carbon, dissolved ozone, APEOs, nonylphenol (NP), and octylphenol (OP). Samples of aqueous environmental matrices were collected from effluent mains from a hospital and wastewater treatment plant, an influent main from a wastewater treatment plant, and a buildings potable water tap using a peristaltic pump with teflonated tubing. 10-L samples of each aqueous environmental matrix were collected into polypropylene bottles, stored on ice for transport back to the testing laboratory, filtered through 1 μm glass fiber filters, and used in the experiments with molecular ozone.

4.2.4 Analysis of APEOs and APs

Aqueous solutions from all semi-batch and batch experiments produced during the kinetic studies were transferred to 1-L amber glass bottles and sent to US EPA

Region 5's Central Research Laboratory (R5CRL) for NPEO and OPEO analysis. APEOs were extracted and analyzed following US EPA R5CRL's standard operating procedure MS006 V1, which is described in a previous publication [66]. The APEO method utilizes solid phase extraction to remove the analytes from the matrix, an Atlantis ™ MS C_{18} column (150 mm x 2.1 mm x 3 μm) to chromatographically resolve the analytes on column, and a Waters 2659 liquid chromatography (LC) coupled with a single quadrapole ZQ mass spectrometer operated in positive electrospray ionization mode under atmospheric conditions. A five point external calibration and single ion recording (SIR) is used to quantify the target analytes.

NP and OP analyses were accomplished by a 25-μL injection of reactor sample onto a 5-μm, 4.6 mm x 100 mm Hypersil Green PAH column on the front end of a Thermo Surveyor LC equipped with a diode-array detector. The two compounds were separated on column using a 70:30 acetonitrile:0.2% acetic acid in water isocratic eluent system at a flow rate of 1 mL/min. NP and OP were detected at a wavelength of 224 nm and quantified using a five point external calibration curve.

4.2.5 Degradation product identification

Degradation products were qualitatively identified using a Finnegan LCQ Deca XP Max Ion Trap system operated in positive electrospray ionization mode under atmospheric pressure. Analytes were introduced on column with a 25-μL full loop injection and were separated on a 5-μm, 4.6 mm x 100 mm Hypersil Green PAH column. A 70:30 acetonitrile:0.2% acetic acid in water isocratic eluent system with a 0.5

mL/min flowrate was used to chromatographically resolve the analytes. The MS^n system was tuned on the parent compound (OPEO or NPEO) and operated using full scan mode with an m/z range from 250 to 800.

4.2.6 Total organic carbon and dissolved ozone

Standard Method 5310B was followed to determine the dissolved organic carbon concentration within samples on a Shimadzu 6000V TOC Analyzer [98]. Dissolved ozone was monitored by an online analyzer using a Q45H Dissolved Ozone Monitor. The monitor was calibrated by measuring dissolved ozone following Standard Method 4500 (ozone - indigo method) [98, 115].

4.3 Results and Discussion

4.3.1 Kinetics of molecular ozone consumption

Ozone consumption in the presence of excess APEOs was monitored at pH 3 and 6 utilizing the batch reactor system. Figure 4-1 presents the consumption of ozone over time within the batch reactor system during oxidation of OPEO and NPEO. Pseudo first-order rate constants for molecular ozone consumption (k'_{O_3}) in the presence of NPEO and OPEO were estimated to be 0.056 and 0.038 s^{-1}, respectively and the kinetic rate constants were not dependent upon pH under acidic conditions.

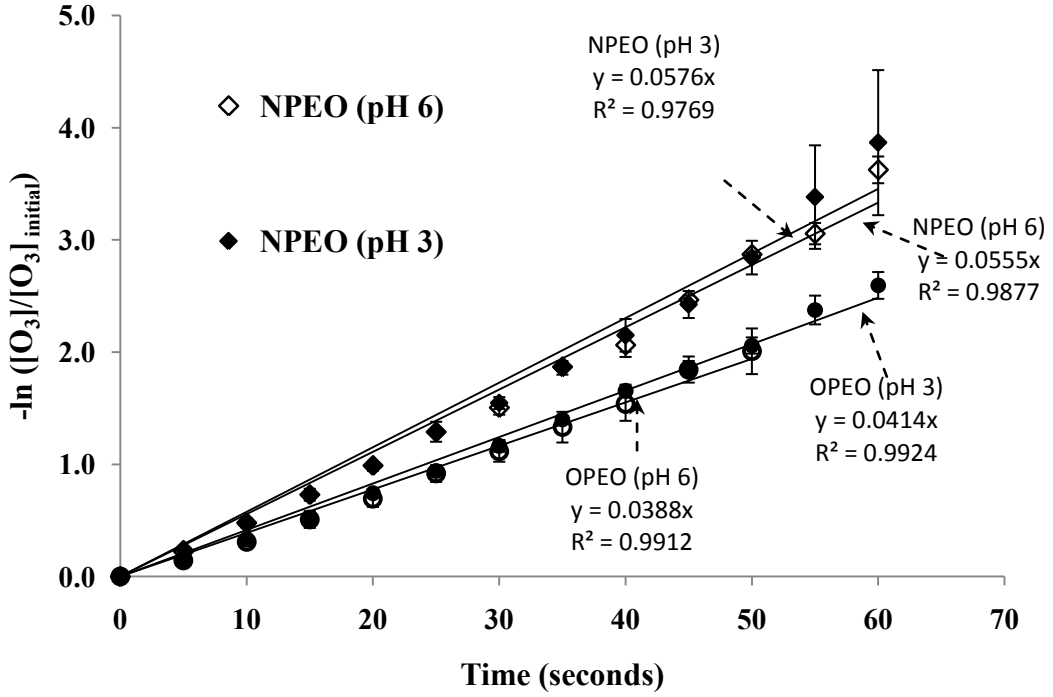


Figure 4-1 Ozone consumption during the reaction of molecular ozone with NPEO and OPEO in ultrapure water within a batch reactor system

Ozone self degradation was also monitored for three minutes prior to spiking APEOs into the reactor to start the experimental run. The rate of ozone self degradation increased from $3.0x10^{-4}$ to $6.0x10^{-4}$ s^{-1} in ultrapure water with an increase in pH from 3 to 6. The solution pH was kept below 6 and a scavenger was added to limit hydroxyl radical formation so molecular ozone could be studied in isolation. However, the self degradation rate of ozone within the reactor was negligible (2 orders of magnitude lower) compared to the ozone uptake associated with oxidation of APEOs at both pH levels. Providing APEO in excess within the batch system also limited the reaction between ozone and APEO degradation products.

The second-order rate constant for ozone consumption (k_{O_3}) was estimated based on the initial concentration of NPEO or OPEO in solution and the pseudo first-order rate using the following equation (1):

$$k_{O_3} = k'_{O_3} \cdot [\mathrm{APEO}]_0 \qquad 4\text{-}1$$

The overall second-order rate constant for ozone consumption was $6.0x10^{2}$ and $9.0x10^{2}$ $M^{-1}s^{-1}$ for OPEO and NPEO. There is limited literature available regarding the second-order rate constant of ozonation of ethoxylates. Bader and Hoigné (1981) reported values for ozone consumption during the oxidation of phenol as $1.3x10^{3}$ $M^{-1}s^{-1}$. Based upon our experimental data, the presence of the ethoxylate group reduces the second-order rate constant less than an order of magnitude.

4.3.2 Kinetics of APEO oxidation with molecular ozone

Ozonation experiments were performed in a semi-batch reactor to determine the second-order rate constant for the oxidation of APEOs (k_{APEO}) by measuring the loss of APEO in solution. Within the semi-batch experimental setup, the overall reaction is controlled by both the transfer of ozone from the gas phase to the liquid phase (mass transfer limited) and the reaction between ozone and the organic compounds in the water (chemical reaction limited). As a result the overall rate of reaction can be limited by chemical kinetics, mass transfer, or a combination of both factors.

The semi-batch reactor was operated under kinetically limited conditions for each experiment (observed as a buildup of dissolved ozone in solution). The second-order rate constant was calculated for total NPEO and OPEO by plotting $\ln([APEO]/[APEO]_o)$ as a function of ozone exposure ($\int_0^t [O_3]dt$). The overall rate constant obtained from the slope is independent of analyte initial concentration, ozone concentration, and time of the reaction as has been described by equation (2):

$$\ln\left(\frac{[APEO]}{[APEO]_0}\right) = k_{APEO} \cdot \int_0^t [O_3]dt \qquad 4\text{-}2$$

The overall second-order rate constant for OPEO and NPEO (k_{APEO}) was determined as 1.3 x 10^2 and 3.06 x 10^2 $M^{-1}s^{-1}$, respectively (regression coefficient (r^2) above 0.95 for both APEOs). Ning *et al*. (2007) [105] previously reported second-order rate constants as 4.3x10^4 and 3.9x10^4 $M^{-1}s^{-1}$ for octylphenol and nonylphenol, respectively. A comparison of the second-order rate constants for APEOs and APs indicates that the presence of the ethoxylate groups reduces the resulting rate constant by

up to two orders of magnitude. Therefore, a higher ozone exposure is required to eliminate APEOs compared to APs.

4.3.3 Determination of the stoichiometric factor

The two rate constants, k_{O_3} and k_{APEO}, are based on two different types of measurements. k_{O_3} is calculated by measuring the consumption of ozone in the presence of excess APEO, a pseudo first-order reaction, while k_{APEO} is obtained from measuring the consumption of APEOs in the presence of molecular ozone. The two rate constants are related by the stoichiometric factor according to equation (3) [104]:

$$k_{O_3} = \gamma \cdot k_{APEO} \qquad 4\text{-}3$$

Based upon this equation and the kinetic rate constants determined through experimentation, the stoichiometric coefficients (γ) for NPEO and OPEO were calculated to be 2.95 and 4.62, respectively. These findings agree with previously reported stoichiometric coefficients for the reaction of molecular ozone with organics [104, 114]. The reaction stoichiometry ($1/\gamma$) indicates that 0.34 moles of NPEO are reacted per mole of ozone consumed as compared to 0.22 moles of OPEO reacted per mole ozone consumed. The difference in observed reaction stoichiometry likely occurs due to the difference in the average ethoxylate chain length (10 for OPEO and 15 for NPEO), the ethoxylate chain length distribution (4-12 for OPEO and 9-18 for NPEO), and the resulting molecular weight differences (646 for OPEO and 820 for NPEO) between the two APEOs.

4.3.4 Ozonation and product formation

Figure 4-2 shows the decrease in concentration observed for APEO of different ethoxylate chain length with 1 and 15 minutes reaction. Concentrations of APEOs of all ethoxylate chain lengths decreased during the course of the reaction without the formation of APEOs with shorter chain ethoxylates as degradation products. However, during the process of monitoring for the two APs, a degradation product peak was observed in the LC-diode array detector system that required further investigation with LC/MS^n for identification purposes. Figure 4-3 presents the results of the LC/MS^n degradation product investigation and the resulting proposed pathway of the initial oxidation of APEOs with molecular ozone that was observed in our research.

The *m/z* difference between each individual APEO and the resulting degradation product observed in reaction solution was M+16 or M+32, which are qualitatively identified as M+OH and M+2OH. The M+OH represents a single hydroxyl group addition to the phenolic ring (a catechol derivative) and was observed for all chain lengths of OPEO and chain lengths of NPEO up to 12 ethoxylate units after 15 minutes of reaction with molecular ozone. For NPEOs with greater than 12 units, the M+2OH degradation product was observed; representing a two hydroxide addition the phenol ring. While the M+OH degradation product formation is consistent with previously reported literature for the reaction of molecular ozone with APs [105], the M+2OH degradation product of AP or phenol does not appear in the literature to the best of our knowledge.

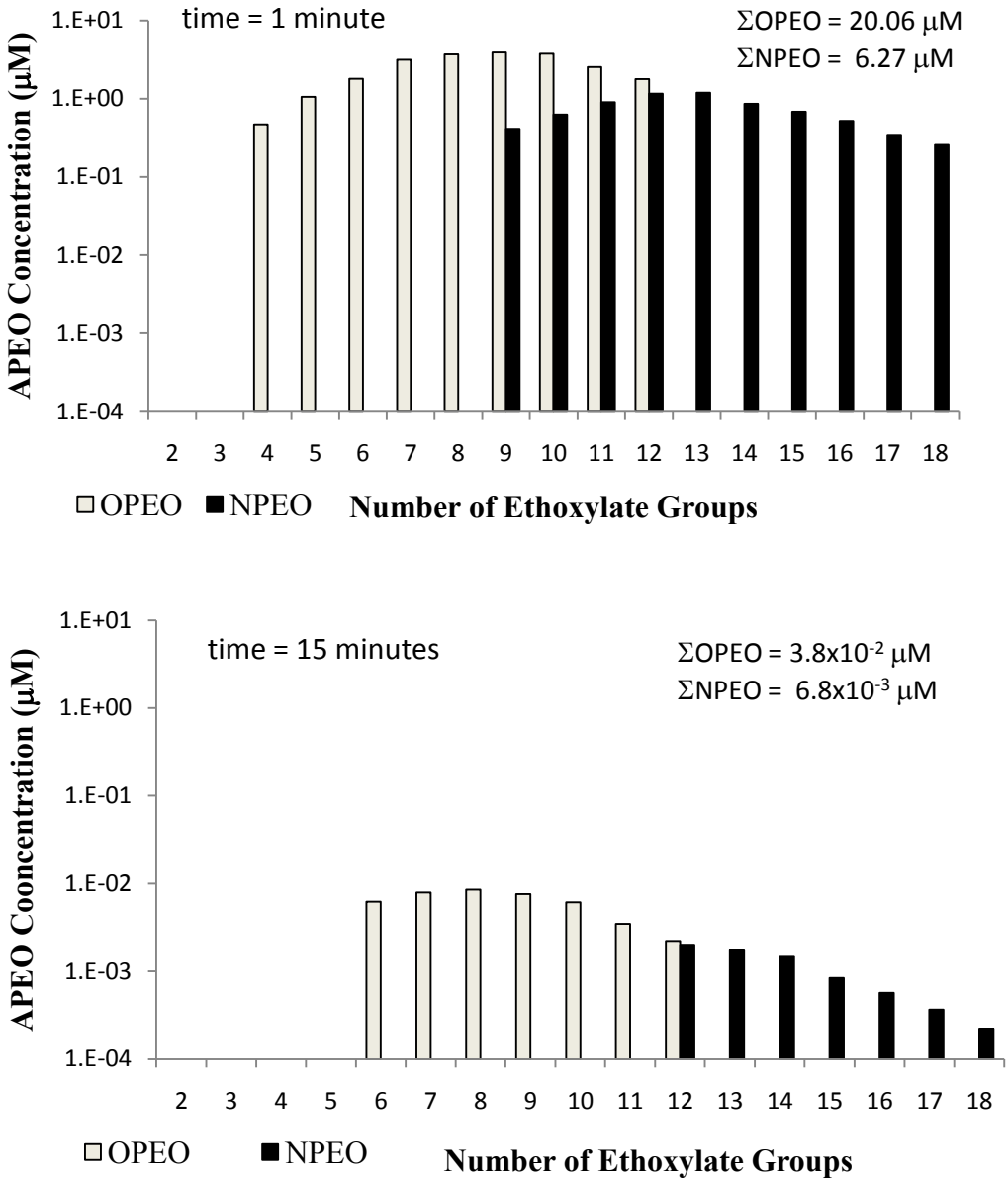


Figure 4-2 Concentrations of individual ethoxylate chains lengths observed after 1 min and 15 min during the reaction of NPEO and OPEO with molecular ozone. Formation of shorter chain APEOs or APs were not observed during the reaction with molecular ozone, however other degradation products are formed.

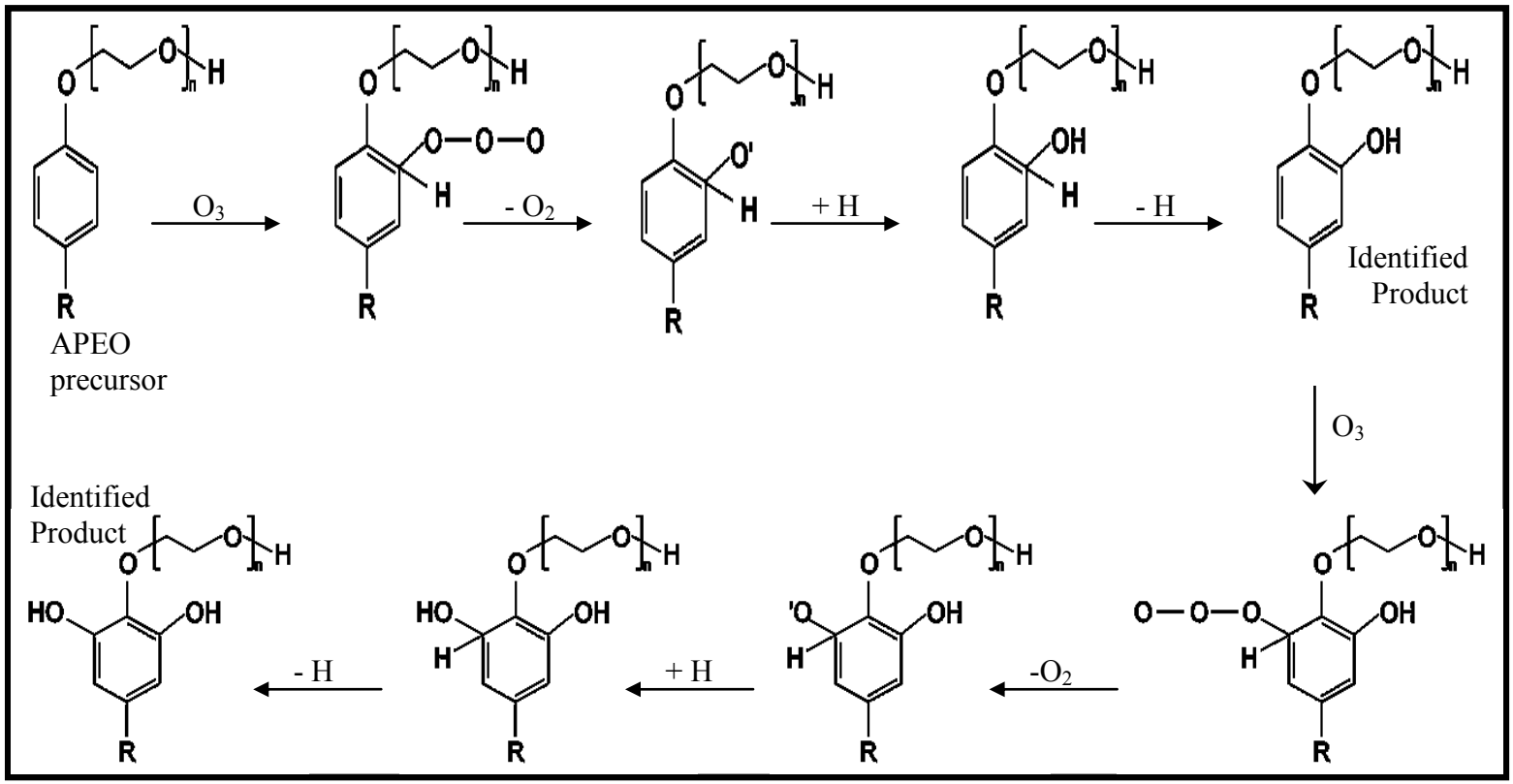


Figure 4-3 Proposed initial reaction pathway during the oxidation of APEOs with molecular ozone

While analytical standards of the products were not available for quantitative analysis for mass balance purposes, the rise of the hydroxylated APEO product peak corresponded to a proportional decrease in APEO observed after 1 minute, 15 minutes, and 30 minutes of reaction.

However, while proportionality was observed, this approach only arrives at a qualitative measure of the transformation of APEO to the hydroxylated APEO degradation product and quantitative analysis of the degradation products is required before a mass balance could be attempted.

4.3.5 Impact of matrix on the effective kinetic rate constant ($k_{APEO,\ effective}$)

The effect of different aqueous environmental matrices on the kinetics of the reaction of APEOs with molecular ozone was studied using the semi-batch reactor system. $k_{APEO_{effective}}$ was calculated based upon the removal of NPEO and OPEO in tap water, wastewater treatment plant effluent, wastewater treatment plant influent, and hospital wastewater effluent. Table 4-1 presents the $k_{APEO_{effective}}$ for each aqueous matrix.

The observed value of $k_{APEO_{effective}}$ determined in each aqueous environmental matrix trends with the amount of dissolved organic carbon (DOC) in the samples. $k_{APEO_{effective}}$ decreased from tap water > WWTP effluent > WWTP influent > hospital effluent and the relationship between $k_{APEO_{effective}}$ was observed to be negatively correlated with DOC based upon a pearson's product moment correlation analysis. However, additional samples need to be assessed to determine if this relationship is

statistically significant at a greater than 75% confidence level as observed with our experimental data.

Table 4-1 Second-order rate constants for the reaction of APEO with molecular ozone in different aqueous matrices. Except for in ultrapure water, the presented second-order reaction rate constant is an effective rate constant

Aqueous Matrix	**Initial DOC**	**Second-Order Rate Constant**	
		NPEO	**OPEO**
	(mg C L^{-1})	($M^{-1}s^{-1}$)	($M^{-1}s^{-1}$)
Ultrapure Water	0.00	1.54E+03	3.89E+02
Tap Water	1.07	3.84E+02	1.90E+02
WWTP Effluent	3.16	0.60E+02	0.10E+02
WWTP Influent	13.25	0.23E+02	0.06E+02
Hospital Effluent	33.94	0.10E+02	0.03E+02

The observed trend follows previously literature reports demonstrating the reduction in reaction rate constants for other trace organics in the presence of DOC [20, 96, 104, 107]. As a consequence, ozonation of water and wastewater with higher organic loadings will result in slower trace organic removal than kinetic studies performed in laboratory waters unless a higher ozone exposure is administered.

4.3.6 Impact of ozonation as a potential pretreatment process

The primary concern of APEOs in wastewater is that they can degrade into APs due to biodegradation processes occurring in municipal wastewater conveyance and treatment systems [48, 81, 83]. APs are known to bind to the estrogen receptor in exposed organisms and are recognized as endocrine disrupting compounds. A pretreatment technology that can remove APEOs before their relase from a source can therefore eliminate the potential estrogenicity of the water or wastewater due to the degradation of APEOs to APs. At first glance, molecular ozone does appear to remove NPEO and OPEO from the aqueous matrices. However, the formation of hydroxylated NPEO and OPEO degradation products may not actually prevent the biodegradation of APEOs into APs over time. The degradation products also may have EDC effects greater than their precursor.

Progressive fragmentation of the polyethoxylated side chain by hydrogen abstraction followed by depolymerization is suggested in the literature [116], however progressive fragmentation was not observed in the presence of molecular ozone within this study. The observed formation of hydroxylated APEO products in our experiments is due to ozone's specificity for double bonds within the aromatic ring [103, 112].

Opening of the ring during ozonation of phenol and APs is also suggested in the literature [105, 117]. While ring breakage through product screening analysis was not evident based upon our analytical methods used for identification of transformation products, ring breakage would be preferable because the phenolic ring is responsible for the observed estrogenicity of APs [38, 85, 86, 108]. Based upon the experimental data produced during this research, the slow reaction rates and formation of structurally similar degradation products during the reaction suggest that molecular ozone by itself would not be a suitable pretreatment process for NPEOs and OPEOs. Ozonation carried out at a higher pH or incorporated into an advanced oxidation system, such as ozone/hydrogen peroxide, should lead to faster reaction kinetics without the observed formation of hydroxylated APEO degradation products due to reactions with the hydroxide radical. Use of ozone in a way that promotes formation of the hydroxyl radical is a more preferable approach for pretreatment of APEO in aqueous systems.

5. CONCLUSION

The aim of this dissertation was to perform research needed for risk management of PPCPs in healthcare facility wastewaters. The two broad hypotheses investigated to achieve this aim. Hypothesis 1 was "Healthcare facilities are a source of PPCPs to municipal wastewaters" and Hypothesis 2 was "Chemical oxidation processes can be used to remove APEOs from water and wastewater". Screening-level analytical studies were carried out on effluents from four healthcare facilities to determine the composition and magnitude of 94 individual PPCP analytes present in the wastewater leaving each facility in order to evaluate Hypothesis 1.

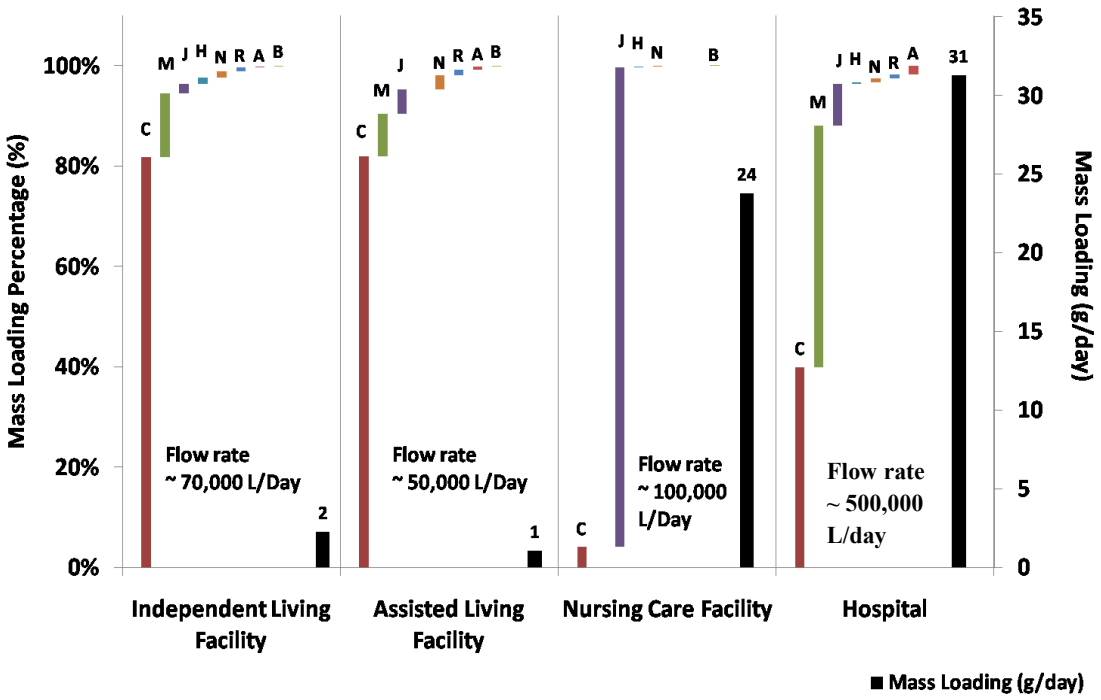
Based upon the results of the source characterization study, APEOs were selected as the test chemicals to evaluate chemical oxidation options that could be used in pretreatment systems for healthcare facility or industrial process waters. Three advanced oxidation processes (UV – hydrogen peroxide, Fenton's process, and photo Fenton's process) and molecular ozone were investigated to elucidate the OH· and molecular ozone reaction kinetics with APEOs, to investigate degradation products formed during the oxidation process, and to explore impacts of different aqueous matrices on reaction kinetics.

The primary findings of research directed toward evaluating Hypothesis 1 include: 1) PPCPs are present and identifiable in healthcare facility effluents, 2) each sampled facility wastewater exhibited different PPCP concentrations and mass loadings based upon the type of medical services provided within the facility and the health of the

patients; 3) of the 94 individual analytes measured in this research APEOs were the dominant PPCP class accounting for more than 65% of the total mass loading observed leaving three of the four facilities; and 4) healthcare facilities are a source of PPCPs to the environment, but their contribution to the magnitude of PPCPs in municipal wastewater and the surrounding environment will be determined by the location of the healthcare facility within a wastewater conveyance system and the flow of wastewater released from the facility.

Seventy-one out of the 94 measured pharmaceutical analytes were detected in wastewater from at least one facility during the research and the concentrations ranged from below 1 nanogram per liter to hundreds of micrograms per liter. The differences in pharmaceutical composition observed in the healthcare effluents and the mass loadings of total pharmaceuticals are shown in Figure 5-1. It is interesting to point out that 12 of the pharmaceuticals were observed in at least one facility's wastewater at concentrations greater than 1 μg/L. In comparison, every APEO detected in facility wastewater was present at concentrations above 1 μg/L with a maximum observed NPEO concentration of 260 μg/L in the assisted living facility wastewater. Because APEOs were present at high concentrations when detected, APEOs in three of the four sampled facilities dominated the overall PPCP composition as shown in Figures 5-2. Only the nursing home wastewater was not dominated by APEOs and this is likely because the linens at the faculty were laundered off-site (although we never did confirm this plausible explanation).

While the source characterization data provided by this study clearly shows the presence of PPCPs in healthcare effluents, the overall importance of healthcare facility PPCP release compared to other sources within a municipal wastewater system is difficult to establish. Assessing the PPCP inter-facility variability and temporal variability needs to occur as part of future work to determine the importance of healthcare facilities as PPCP sources to municipal wastewaters.



The letter corresponds to ATC code for pharmaceuticals

Figure 5-1 Composition of pharmaceuticals present in each facility wastewater along with the estimated mass loading of total pharamceuticals leaving each facility through effluent discharges to the municipal wastewater system

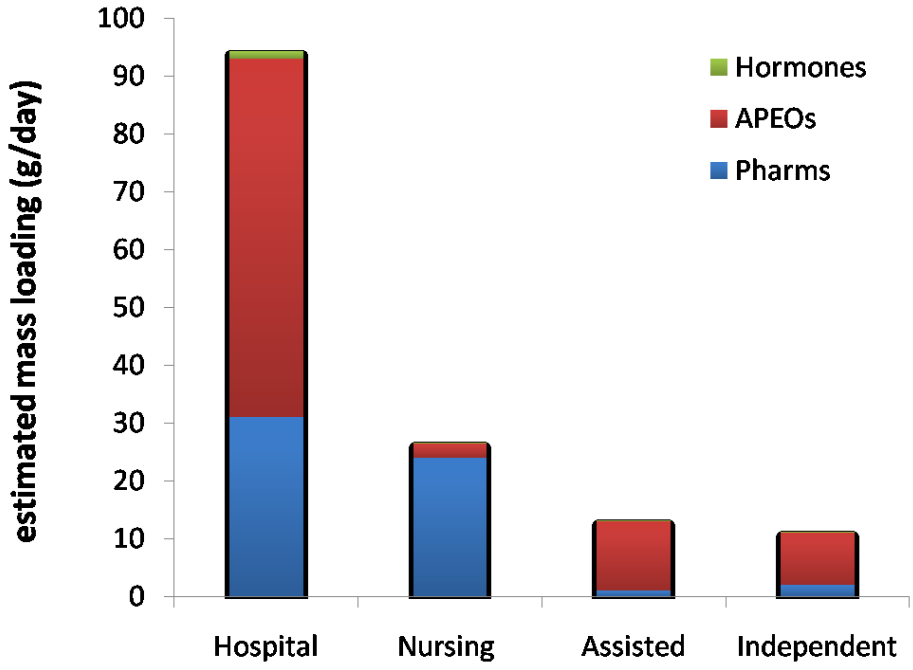


Figure 5-2 Contribution of pharmaceuticals, APEOs, and hormones to estimated total PPCP daily mass loading from each facility type

Additionally, knowledge of the wastewater flows within a given municipal wastewater system is also essential to assessing the overall importance of any facility to PPCP loadings to the municipal wastewater conveyance systems. In the sampled municipality, the four healthcare facilities that were sampled contributed only 0.2% of the total wastewater flow treated by the municipal treatment plant. In the case of this municipality, the municipal wastewater flow will dilute out the signal from each facility. However, one can easily envision situations where a large healthcare facility could dominate wastewater flow in small municipal systems. Where these situations arise, risk management approaches should be considered. Impacted municipal treatment facilities could rely on source reduction approaches and on onsite pretreatment to reduce the loading of PPCPs passed to the municipality's treatment facilities instead of upgrading its capabilities.

Research directed toward evaluating Hypothesis 2 provides an initial dataset that adds to the discussions concerning pretreatment as a risk management approach for PPCPs that are currently occurring within EPA as a result of our source characterization work. An evaluation of chemical oxidation processes with a focus on their potential implementation as pretreatment technologies (or even potentially as a tertiary treatment approach at wastewater plants) was explored. APEOs were selected as test chemicals because of 1) their abundance in the sampled healthcare facility wastewaters; 2) the fact that APEOs degrade to APs during wastewater conveyance and treatment (which leads to endocrine active degradation products); and 3) the absence of experimental data in the literature on the treatment of APEOs by chemical oxidation processes.

As part of this research, chemical oxidation systems were screened and evaluated as potential pretreatment technologies to remove APEO from water and wastewater. The two main oxidative technologies explored used ozone and hydroxyl radicals as oxidants. The hydroxyl radicals were produced by AOPs that used hydrogen peroxide. Hydrogen peroxide and ozone are easy to implement in pretreatment systems, either as part of a continuous flow through reactor system. The UV-H_2O_2 AOP was the primary focus of research in order to gain information on the AOP process that appears most feasible for implementation as a pretreatment technology. Therefore, the UV-H_2O_2 system was used to understand the reaction kinetics and degradation product formation during the reaction of APEOs with OH· in ultrapure water. Fenton's and photo Fenton's were then explored due to interests in generating basic scientific data missing from the literature. Also, to evaluate if Fenton's would have a higher rate of reaction than UV-H_2O_2 system and if secondary reactions would occur with iron as it is present in the conveyance system or wastewater if UV-H_2O_2 was employed in practice.

Because the investigated AOPs produce OH· , which is responsible for the non-selective oxidation of target organics, we were also interested in learning about the performance of a selective oxidant that could be used to particularly degrade the phenolic ring within APEO. The phenolic ring is responsible for the estrogenic activity of the molecule and breaking the ring would be a successful approach to removing the environmental concern of APEO in wastewaters. Molecular ozone was selected based upon its selectivity for reactions with aromatics and due to previous suggestions in the literature that pointed towards ring cleavage when molecular ozone reacted with phenol

and APs. Laboratory experiments focused on the reactivity of molecular ozone with APEOs, because ozone also leads to the formation of OH· at higher pH ranges and the reactivity of OH· with APEO had been explored through investigation of the UV-H_2O_2 system. By controlling the solution pH and adding OH· scavengers, the molecular reactivity of ozone could be studied in isolation.

Important findings from the oxidation studies include 1) both AOPs and molecular ozone were able to remove APEO from aqueous environmental matrices, 2) understanding degradation product formation is critical to selecting a suitable treatment process, 3) using AOPs at a wastewater source will require higher oxidant loadings to overcome competition of DOC with the oxidant, 4) UV-H_2O_2 and ozone (particularly a ozone-H_2O_2 system) have application as a pretreatment technology for PPCPs in healthcare facilities, and 5) UV-H_2O_2 could be implemented at the full plant scale to achieve removal of PPCPs from effluents.

Both the evaluated AOPs and molecular ozone removed APEO from ultrapure water and actual environmental samples. However, the second-order kinetic rate constant for OH· reaction with APEO was 7 to 8 orders of magnitude higher than the second-order rate constant for the reaction of molecular ozone with APEO. Additionally, while no difference was observed between NPEO and OPEO reactivity towards OH·, there was an observed difference in the reactivity of NPEO and OPEO with molecular ozone; hinting at the difference in reaction mechanism between OH·-APEO and molecular ozone-APEO.

For OH· reaction, the resulting ethoxylate chain length profile during the reaction showed the formation of shorter ethoxylate chain length APEOs not present in the original spiked mixture indicating fragmentation of the ethoxylate moiety. However, OH· reaction with APEOs rapidly decreased the overall APEO concentration and the amount of shorter chain APEOs formed during the reaction also were reduced as a function of reaction time. For molecular ozone's reaction with APEO, the ethoxylate chain length profile during the course of reaction with ozone did not change with time (fragmentation of APEO chain lengths was not observed). However, the reaction of molecular ozone with APEO produced hydroxylated APEOs as a predominant degradation product. While the amount of hydroxylated APEOs was not able to be quantified due to lack of appropriate analytical standards, the rise of the degradation products appeared proportional to the decrease of APEO in solution. Therefore, molecular ozone is not likely to be a useful pretreatment technology for APEOs as APEOs are transformed but not completely removed.

The effect of real aqueous environmental matrices on the removal of APEOs is similar whether OH· or molecular ozone is used. Dissolved organic carbon was the major factor contributing towards the decline in fractional removal of APEOs. Therefore, aqueous environmental matrices with higher DOC content will have lower fractional APEO removal when the same oxidant loading rates are utilized. For OH· reactions, the OH· formation rate by an AOP and the OH· scavenging rate constant by a given matrix can be used to design a treatment process to achieve a given removal of APEO by using the modeling approach presented in Section 4. This approach will prove

useful if AOPs are implemented as treatment technologies for PPCPs in wastewater either at a source (in the effluent line of a hospital for instance) or as a last polishing step for municipal wastewater effluents (introducing H_2O_2 right before existing UV disinfection systems would be an easy addition).

Collectively, our research carried out to evaluate Hypothesis 2 informs risk management decisions concerning the use of oxidation systems as treatment technologies for PPCPs. However, *whether or not to treat* and *where to treat* are additional questions worth discussing. Based upon our research, deciding *whether or not to treat* is not determined by available technologies, but rather social political factors that are currently driven by economics and public interest. Justifying an extensive change of infrastructure to remove PPCPs from municipal wastewater is not feasible. However, if small adaptations can be made or source pretreatment could be brought on-line at low cost, we conclude *why not treat*? While pollution prevention measures are required for industrial producers of PPCPs, large facilities using and releasing high amounts of PPCPs to municipal wastewater should also be required to treat their wastewaters or to pay for upgrades of the municipal treatment plant that receives their wastewater discharge.

If pollution prevention measures point towards treatment, the question becomes *where to treat*? The location of the treatment technology will impact both the efficiency of any proposed technology and the cost of implementation. Treated wastewater effluents have lower DOC content compared to healthcare facility effluents, so treatment process efficiency may make up for the difference in cost caused by the scale of

treatment required between an individual facility and the total wastewater flow in a given municipal system. Additionally, many wastewater treatment plants are now equipped with UV reactors for disinfection purposes and adding H_2O_2 may not significantly enhance capital or infrastructure costs. In the end, economic feasibility will actually drive the decision on where to implement the removal technology. Performing such an economic feasibility assessment would be a nice addition to our knowledge base that could be accomplished using the data presented in this dissertation. Additionally, it is hoped that this research will be used by municipal utility manager, regulators, and facility managers to determine if risk management approaches to reduce PPCPs in healthcare facility wastewaters within their jurisdiction should occur.

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